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# VISUALIZATION OF THE CHAMBERS OF THE HEART, THE PULMONARY CIRCULATION, AND THE GREAT BLOOD VESSELS IN MAN*†

## A PRACTICAL METHOD

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HERETOFORE there has been no method of visualizing the left chambers of the heart and the superior vena cava and no practical procedure for outlining the right chambers of the heart, the pulmonary circulation and the thoracic aorta in man. Gross changes in size and shape have been detectable by roentgen examination but precise information concerning the individual chambers of the heart, the pulmonary artery, the vena cava and the aorta could not be obtained. Contrast roentgenography has made such information available in other regions of the body, notably the central nervous system, the bronchi, the gastrointestinal tract, the genitourinary system, and the peripheral arteries and veins; but this method has had limited success when applied to the cardiovascular structures in the thorax. Forssmann[11] in 1931 tried unsuccessfully to visualize the chambers of the heart by the injection of an iodide preparation into the right auricle through a catheter which he had introduced into a vein at the elbow and advanced to the heart. In the same year Egas Moniz, Lopo de Carvalho and Almeida Lima[9] succeeded in visualizing the pulmonary blood vessels by the use of a concentrated solution of sodium iodide and Forssmann's technique of injection. Since then, this method of pulmonary arteriography or modification has been used by Lopo de Carvalho and his associates,[25,26,27,28] Conte and Costa,[5] Heuser,[15] Ravina,[37] and others. Ameuille and his associates[1] also outlined the right chambers of the heart in this way in a few instances. Although reputedly harmless, the difficult nature of cardiac catheterization has precluded general use of this method. Nuvoli[33] recently made the thoracic aorta opaque by injecting sodium iodide after puncturing the left ventricle in one patient and the ascending aorta in another; this technique obviously is not suitable for routine use. In the past year, Castellanos, Pereiras, and Garcia[4] visualized the right side of the heart and the pulmonary artery by the peripheral intravenous injection of organic iodide compounds. Their method, however, was effective only in children under six years of age and it failed to outline the left chambers of the heart and the aorta.

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Intravenous injection of the radiopaque substance for visualization of the pulmonary blood vessels in adults has been tried and discarded.[26] Despite these failures, it was believed that opacification of the heart and the lungs could be accomplished in this way because of the relatively high concentration with which brilliant vital red dye traverses these structures in the dye injection cardiac output method.[29,50] In order to test this belief it was necessary, first, to develop a technique which would permit injection of the radiopaque substance rapidly enough to make the blood stream opaque, and then to find a contrast solution which would be freely miscible with the blood, pharmacologically inert, nonirritating to the vascular system, nontoxic in the dosage used, and rapidly inactivated or eliminated by the body. The use of a large bore needle and syringe tip permitted the ejection of 30 cc. of water per second, a rate which later was found sufficient to satisfy the first requirement. The relatively innocuous organic iodide compounds used for intravenous pyelography offered a possible solution for the other problem. Preliminary study in rabbits begun in January, 1936, showed that visualization could be obtained by the use of several of these compounds in amounts comparable to those which could be given safely to man, and that the addition of glucose[3] or sodium iodide[5] was unnecessary. Clinical trial then proved the feasibility of this procedure[39]; the first successful visualization of the right side of the heart and the pulmonary circulation was obtained on January 30, 1937, and the first visualization of the left chambers and the aorta on May 23, 1937.

## METHOD

The method consists of two essential parts: the injection of enough radiopaque substance into the blood entering the heart to make the chambers and important thoracic blood vessels opaque to the roentgen ray during the first circulation; and the making of roentgenograms of these structures at the time of opacification.

The procedure is carried out in two stages. In the first, a large transfusion needle is inserted into the basilic or cephalic vein of the arm. The patient then is seated before the casette in the position giving the best view of the structures to be visualized; this position should be determined beforehand by roentgenoscopic examination. The arm used for the injection is extended upward and the radiopaque solution is injected rapidly into the vein. Roentgenograms are made after appropriate intervals. The intervals between injection and the arrival of the contrast substance in the superior vena cava, the right chambers of the heart, and the pulmonary blood vessels are short and fairly constant. Longer and more variable periods are required for it to reach the left chambers of the heart and the thoracic aorta, but they may be learned before injection by determining the circulation time to these regions.

Low power roentgen-ray equipment can be used although a power unit with high capacity gives better results and is therefore desirable. A fast moving stereoscopic casette shifter is advisable because it provides two roentgenograms per exposure, and also stereoscopic films if desired. Two operators are required: the physician, who makes the injection, and the technician, who makes the roentgenograms and assists in other parts of the technique.

*Solutions:*

(1) 70 per cent aqueous solution of diodrast.*
(2) 0.9 per cent solution of sodium chloride.
(3) 2 per cent solution of procaine hydrochloride.
(4) 1–1000 solution of epinephrine hydrochloride.
(5) 2 per cent aqueous solution of sodium cyanide.
(6) Ether U. S. P.

*Apparatus* (see Fig. 1):

(1) Needles:
1 needle-stopcock unit:† a modified 12-gauge Lindemann transfusion needle connected to a two-way Luer-Lok stopcock having an inside

* Made by the Winthrop Chemical Co., Inc. In the beginning this solution was prepared by concentration of the commercial 35 per cent preparation to 70 per cent by evaporation in a distillation flask. Recently the sterile 70 per cent solution having a pH of approximately 7.4 has been prepared by the manufacturer and provided for this study.

† Made by Becton, Dickinson and Co.

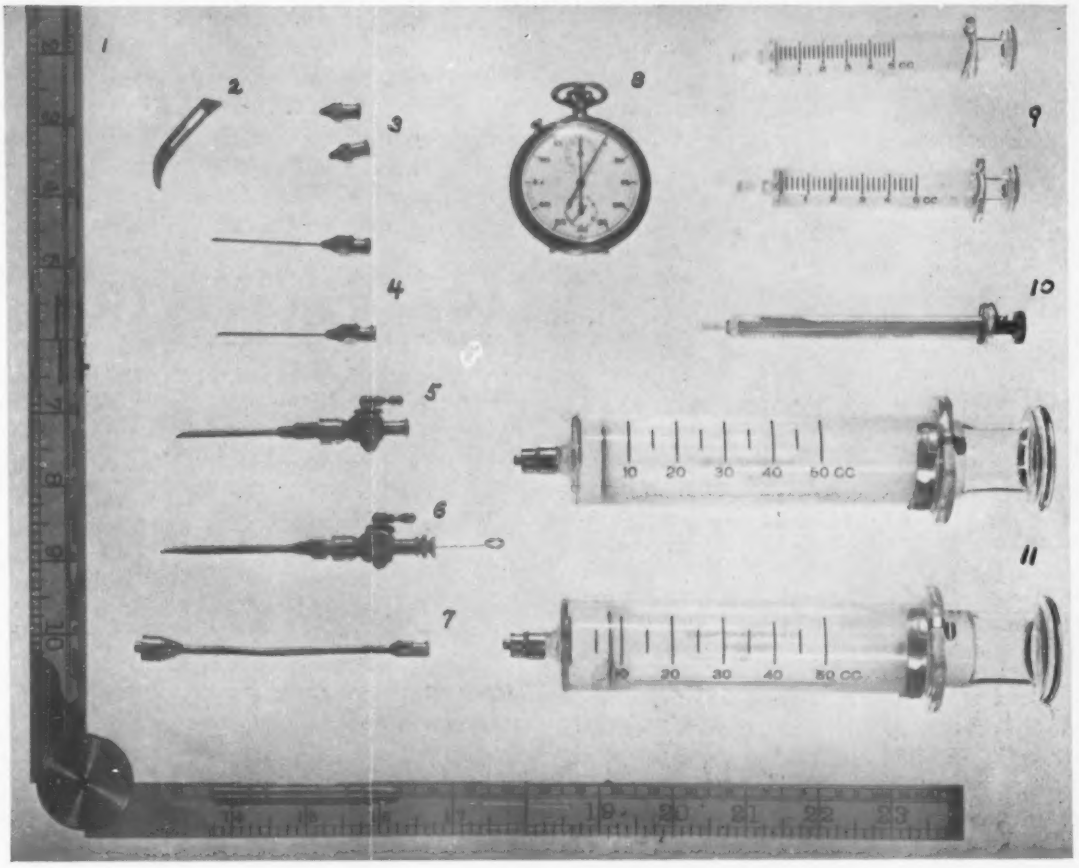


Fig. 1. Apparatus: *1*, protractor rule; *5*, 12-gauge bevelled point transfusion needle and two-way Luer-Lok stopcock unit (used originally and in majority of injections; replaced recently by No. 6); *6*, 12-gauge modified Lindemann needle-stopcock unit; *7*, flexible metal adapter; *11*, 50 cc. Luer-Lok syringe with 12-gauge tip.

diameter of 0.083 inches (12-gauge) instead of the standard 0.054 inches.* The outer cannula is 1½ inches long and remains attached to the stopcock. The inner cannula and needle, which are fused together, extend through both stopcock and outer cannula.

2 18-gauge needles, 2 inches long—for the transfer of diodrast and other solutions.

2 26-gauge hypodermic needles, ½ inch long.

(2) Syringes:

2 50 cc. Luer-Lok syringes with 12-gauge tip instead of the standard bore of 0.073 inches.†

2 5 cc. syringes.

1 1 cc. syringe graduated in hundreths of a cubic centimeter.

(3) Bard-Parker knife blade.

(4) Stopwatch.

(5) Roentgenographic equipment:

(a) A power unit having a capacity of at least 300 ma. and 75–100 kv. (peak), and an exposure time of 1/20 second or less at a distance of 72 inches.

(b) A casette shifter requiring 2 seconds or less to shift films.

The following exposure factors can be used but give poorer results: 50 ma., 75 kv. (peak), exposure time 1/5 second, and distance 60 inches.

(6) Lead screen or apron.

(7) Angle meter.‡

(8) Tourniquet, adhesive tape, alcohol, sterilizer, and sterile gauze squares.

*Technique.* Roentgenoscopic examination of the chest usually precedes visualization of the heart and aorta in order to find the optimal position of the thorax for the right and left anterior oblique views. The degree of rotation for each position is measured by means of an angle meter or a revolving stool designed for

* This greater bore increases the cross-sectional area by more than 100 per cent and doubles the speed of injection.

‡ The 2-foot protractor rule made by the Lufkin Rule Co. is satisfactory.

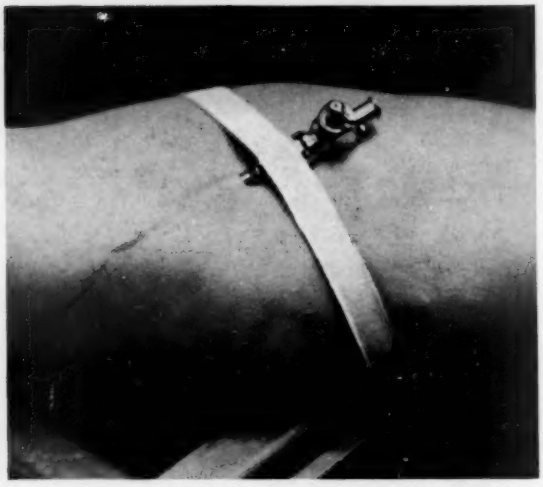

FIG. 2. Arm resting on table during first stage. Needle-stopcock unit in median basilic vein and held in position by adhesive tape. Note alignment of needle and vein. Mark on arm indicates course of vein.

this purpose.* To test the correctness of the position and the roentgenographic technique, a control roentgenogram is made and developed at once. Blood pressure and heart rate are recorded. Epinephrine, 0.3 to 0.5 cc., should be given if allergic tendency, drug sensitivity, or arterial hypotension is present. The apparatus used for injection is sterilized and the sterile solutions of diodrast and sodium chloride are warmed to, and maintained at, body temperature. Hypodermics of procaine and epinephrine are prepared, and a 50 cc. syringe is filled with sodium chloride solution.

The patient now is seated with one arm resting upon a table. Selection of the arm for injection is governed by the position to be used and will be discussed later. A tourniquet is applied to the arm tightly enough to cause intense engorgement of the veins, and the principal vein, preferably one having a diameter of 6 mm. or more, is selected. After anesthetization with 0.2 to 0.3 cc. of procaine solution, the skin at the site of proposed puncture is nicked with the knife blade. The stopcock with the needle attached is grasped in the right hand between the index and middle fingers in front and the thumb behind. The outer end of the stopcock against which the thumb presses is protected by a sterile gauze square. The needle thus held is inserted into the vein and advanced 2 to 3 cm. within the lumen. When venipuncture is successful the gauze square becomes stained with blood. The tourniquet is then released; the combined inner cannula and needle is removed quickly, and the stopcock is closed. The cannula with stopcock is aligned with the vein and fixed in this position by a band of adhesive tape (Fig. 2). To test the adequacy of location of the needle, the 50 cc. syringe containing the sodium chloride solution is attached to the stopcock and the liquid is injected rapidly. Thereafter, needle and vein are flushed with salt solution every three to four minutes to prevent clotting. It is essential that the stopcock should remain closed except when connected to a syringe, and that the arm used for injection should be extended while the needle is in place; if necessary, extension can be maintained by use of a posterior splint or adhesive strap.

The ether arm to pulmonary capillary[20] and the cyanide arm to carotid[43,44] circulation times, when indicated, are determined at this point by adaptation of the original techniques. One-half cubic centimeter of ether is added to 20 cc. of salt solution in a 50 cc. syringe and dissolved by shaking. The arm is elevated and the ether and saline solution is injected rapidly. The interval between the beginning of the injection and the detection of ether on the patient's breath is recorded by stopwatch. The cyanide circulation time method is modified in a similar manner; an effective dose of sodium cyanide, usually 0.3 to 0.4 cc. of the 2 per cent solution, is dissolved in saline solution and injected into the elevated arm. The interval between the start of injection and the onset of hypernea is measured.

The patient then takes his seat before the casette in the desired position, and is held there by a chest band. The sensations to be experienced are described to him by the injector, and the respiratory movements used in the procedure are practiced. The arm for injection is raised to the horizontal and the 50 cc. syringe containing the diodrast is attached securely to the stopcock. To prevent change in position of the needle during withdrawal of blood and injection, the patient's elbow is grasped by the injector's left hand; the fingers support the patient's arm while the thumb anchors the stopcock and needle by pressing them against the arm. Venous stasis is induced again and approximately 20 cc. of blood is drawn into the syringe slowly, to prevent diffusion. Being lighter, the blood rises to the top and later, when the arm is raised, it forms a column above the diodrast. The syringe, still connected to the stopcock, is

* Designed by Dr. I. Seth Hirsch, Department of Radiology, New York University College of Medicine.

held by the injector's right hand; the index and middle fingers straddle the upper end of the barrel, and the thumb presses against the side of the plunger close to the barrel to prevent movement of the plunger until the time for injection. The arm is raised to an angle of approximately 45 degrees above the horizontal and the tourniquet is released (see Figs. 3 and 4).

The patient is now ready for the injection. At the direction, "Breathe OUT," he exhales forcibly until stopped by the command, "Breathe IN." He then inspires quickly, and at the same instant the stopwatch is started by the technician and the injection is begun. The contents of the syringe is injected in two seconds or less. The inspiration usually is completed in two to three seconds but should be finished in one second if the vena cava or right auricle is to be visualized. The inspiratory position is held until the opaque material has arrived in the pulmonary arterial tree and the roentgenogram has been made. Then, at the order, "Relax," the patient exhales passively. The inspiratory position is assumed again shortly before the time of opacification of the left chambers of the heart and the aorta, and is held until the instruction, "Breathe naturally," is given after the last exposure has been made. When the longest interval between injection and exposure is less than 8 seconds, the first inspiratory position should be maintained throughout the procedure. Roentgenograms are made after predetermined intervals. The injector, who stands at the patient's side during the exposures, is protected from radiation by the lead screen or apron.

FIG. 3. Right anterior oblique position, immediately before injection (viewed from the side). Syringe containing diodrast attached to needle-stopcock unit. Note column of blood above diodrast and position of injector's hands.

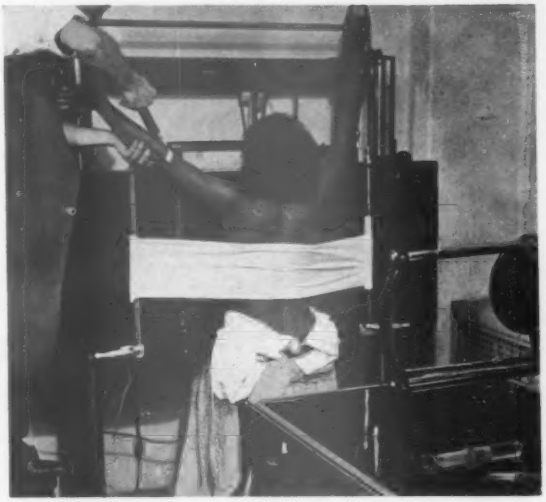

FIG. 4. Posteroanterior position. Note elevation of arms. Injector protected by lead apron stands at side of casette shifter.

After the last exposure, the syringe is disconnected, the chest band is released, and the needle and vein are flushed with sodium chloride solution. The patient is seated again at the table, and the blood pressure and the heart rate are determined while the needle is being removed. Bleeding from the puncture wound is prevented by elevation of the arm and pressure. A sterile dressing is applied and the patient is permitted to leave unless a pyelogram is desired.

*Dosage.* The dosage varies roughly with the body weight and the region to be visualized. In the average person 35 cc. of the 70 per cent solution containing 24.5 grams of diodrast is sufficient for opacification of the left chambers of the heart and the thoracic aorta; 25 to 30 cc., or 17.5 to 21 grams, suffices for visualization of the pulmonary blood vessels. Larger quantities are necessary in patients having thick chests, cardiac enlargement, or pulmonary engorgement. The dosage has ranged from 25 to 45 cc., or 17.5 to 31.5 grams.

*Rate of Injection.* The duration of injection is two seconds or less. This rate of injection offers no difficulty in the average person. In the emphysematous patient, however, in whom the aspiratory action of the thorax is diminished, this rate can be attained only by delaying the injection for one-half to one second after the beginning of inspiration.

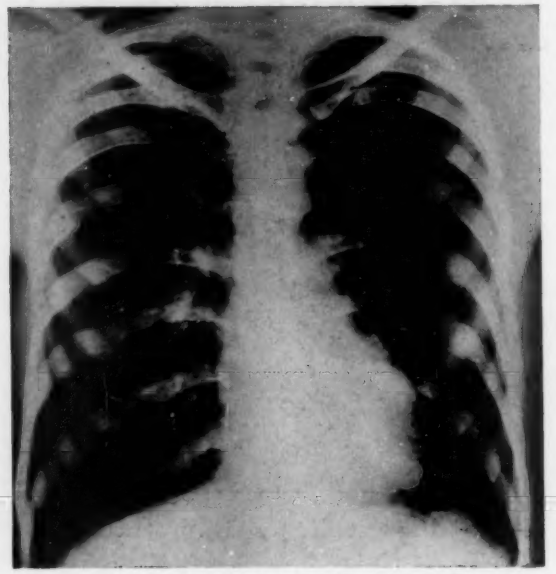

FIG. 5. Normal control.

*Position during Roentgenography.* The posteroanterior position is used routinely for visualization of the superior vena cava, the lung roots, and the pulmonary circulation. The oblique positions are necessary for study of the heart and the thoracic aorta. The left anterior oblique position is used routinely; the right oblique view also is employed when a side view of the heart is desired. The value of each position will be discussed later.

It is necessary to modify the conventional posteroanterior and oblique positions to allow elevation of the arm during injection. In the posteroanterior position both arms are extended upward and outward, thus tending to obscure the apices. Either arm may be used for the injection. When better definition of the apices is necessary, the conventional position in which the shoulders are in contact with the casette can be used, although the technique is more difficult and the injection is slower. In this case the syringe tip is connected to the stopcock by means of a flexible adapter* which is attached to the stopcock and bent upward at a right angle after the patient is in position for the test. Before the syringe is attached, air should be expelled from the adapter by filling it with blood from the vein. In the left anterior oblique position used in this study, the left arm encircles the head in the usual way, but the right arm which is used for injection is extended upward and laterally instead of being flexed with the hand on the hip. In the right anterior oblique position, this procedure is reversed.

*Time for Exposure.* For visualization of the superior vena cava and the right auricle, the time for exposure regularly is one and a half seconds after the beginning of injection. For the right ventricle and the pulmonary arterial tree, the interval is usually three seconds, but may be six seconds or longer if there is pulmonary emphysema or other cause for slow venous inflow. In such patients the appropriate interval should be learned before injection by determining the arm to lung circulation time and subtracting one to two seconds.† The time

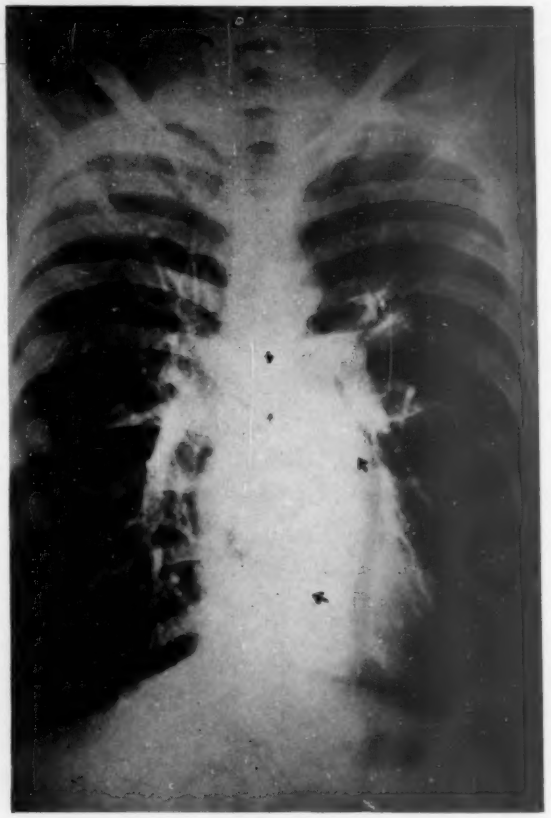

FIG. 6. Contrast roentgenogram. Three seconds after the beginning of injection. Normal, aged twenty. The right chambers of the heart, the pulmonic conus, and the entire pulmonary arterial tree are filled with diodrast. The interventricular septum is indicated by the lower arrow, and the left cusp of the pulmonic valve by the upper arrow. The right branch of the pulmonary artery is bracketed by darts.

* Made by Becton, Dickinson and Co.

† Since this paper was written, experience has shown the advisibility of determining the arm to pulmonary capillary circulation time at least once in every patient in whom the right side of the heart and the pulmonary circulation are to be visualized.

for exposure of the left ventricle generally varies between six and nine seconds with an average of eight, but it may exceed twenty seconds. Because of this variability, it should be determined routinely for each patient before injection. The cyanide circulation time indicates the optimal time for the thoracic aorta, and the left ventricular time is obtained from it by deducting one to two seconds.

*Roentgenographic Technique.* Overexposure is necessary, as in bronchography, to obtain good contrast and definition. An increase of 8 to 12 kv. (peak) in the voltage needed for the conventional film usually suffices. For example, the control roentgenogram (Fig. 5) is that of a patient weighing 112 pounds and having a posteroanterior diameter of the chest of $8\frac{3}{4}$ inches. The exposure factors were: 300 ma.; distance, 6 feet; duration of exposure, 1/20 second, and kv. (peak) 62. In the contrast film (Fig. 6), the kv. (peak) was increased to 70 while the other factors were unchanged. In other respects the roentgenographic technique is identical with that in general use. If stereoscopic films are desired, the interval between exposures must be short, approximately two seconds. More often, the second roentgenogram is used for the visualization of another part of the cardiovascular structure; this is illustrated by Figure 8 which was made five seconds after Figure 6.

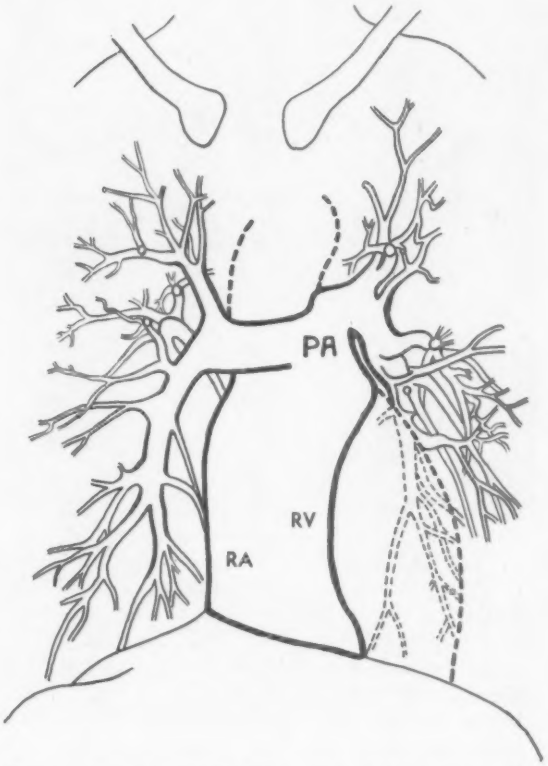


Fig. 7. Tracing of Figure 6. *RA*, right auricle; *RV*, right ventricle; *PA*, pulmonary artery. Note the right and left branches of the pulmonary artery and their numerous subdivisions.

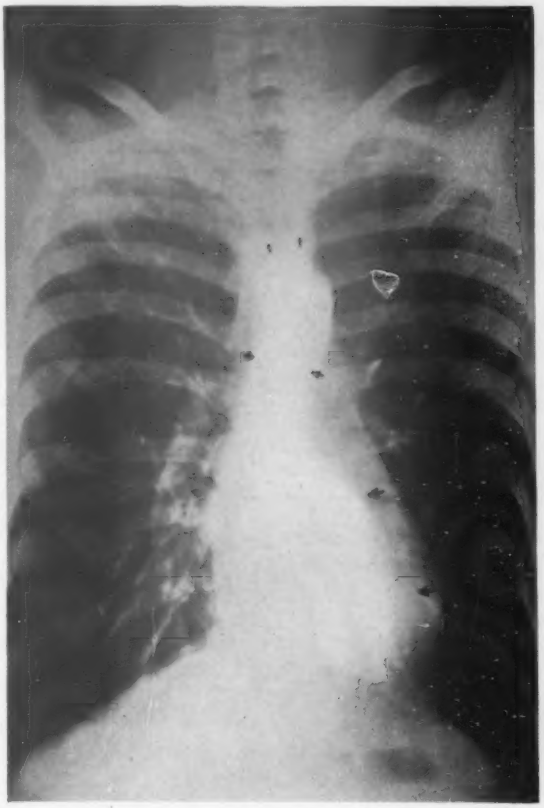

Fig. 8. Same patient as in Figures 6 and 7. Contrast roentgenogram. Eight seconds after injection. The left auricle and the left ventricle are indicated by the middle and lowest arrows on the left side; a pulmonary vein by the lower right dart. The ascending aorta is enclosed by small arrows. Note the two branches from the aortic arch and the left axillary artery.

*Precautions.*

(1) Accepted contraindications to the use of diodrast are severe liver disorders, nephritis and hyperthyroidism.[32] Contrary to general belief,[32] this drug caused no ill effect when given to patients with active tuberculosis. The test should be used cautiously in patients with heart disease and circulatory failure. It should not be used in patients who are critically ill.

(2) Premedication with a barbiturate compound is advisable for extreme nervousness.

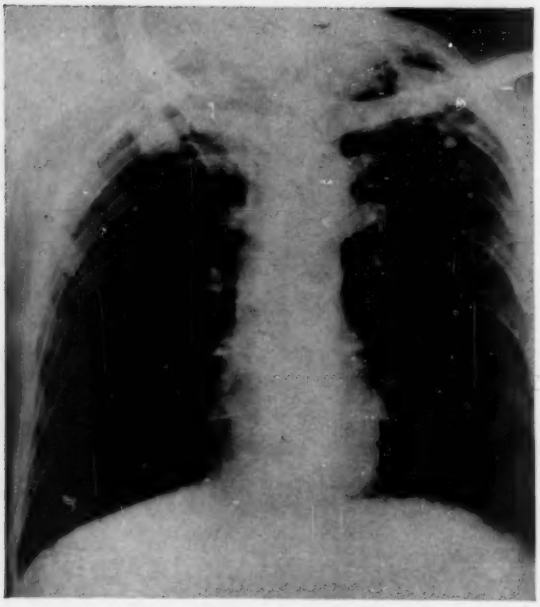

FIG. 9. Control. Productive tuberculosis upper lung fields. Pulmonary blood vessels indistinct.

Epinephrine should be given when there is an allergic tendency or low blood pressure.

(3) A hypodermic of epinephrine should be ready for administration in case of severe reaction.

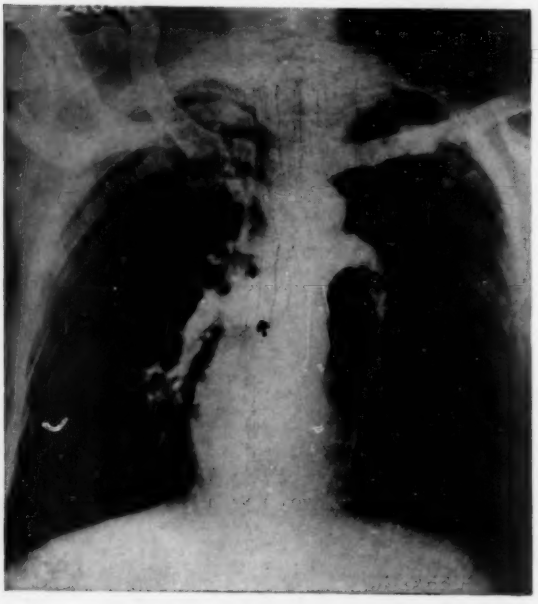

FIG. 10. Contrast film at three seconds. The left branch of the pulmonary artery is pulled up by the tuberculous process. Note the decreased vascularity to the upper lobes.

(4) The stomach should be empty or nearly so to prevent nausea and vomiting.

(5) The sensations to be experienced should be described to the patient to allay apprehension before injection and to prevent excitement during the immediate reaction.

(6) The point and cutting edges of the needle should be sharp, and the vein large and distended until taut, to facilitate venipuncture.

FIG. 11. Contrast roentgenogram. Left anterior oblique position (extreme). Eleven seconds after beginning of injection. Patient, aged thirty-seven, with hypertensive heart disease. Note enlargement of left ventricular cavity and wall (1.7 cm.) and the dilatation and "uncoiling" of the aorta. The lower dart denotes the interventricular septum; the upper three darts indicate the innominate, the left common carotid, and the left subclavian arteries.

(7) The radiopaque solution must be clear and warmed to 37.5° C. If a precipitate is present, the solution should be heated in a water bath until it has dissolved.

(8) Injection must be made only when there is free communication between the needle and the vein. When there is doubt, another vein should be tried or the test postponed.

(9) Vein and needle must be watched during injection to prevent change in position of the needle or overdistention of the vein, and to stop the injection if perivascular infiltration starts.

(10) In case of infiltration, normal sodium chloride solution should be injected immediately through the needle, while it is still in place, to dilute the diodrast and thus lessen irritation.

made. A total of 238 injections was made in 127 patients of whom 42 were normal, 47 had pulmonary disease and 38 cardiac disease. Their ages varied between sixteen and seventy-four. Males predominated, 122 to 5. The number of injections per patient ranged from one to twelve; 20 received three injections or more. Subsequent

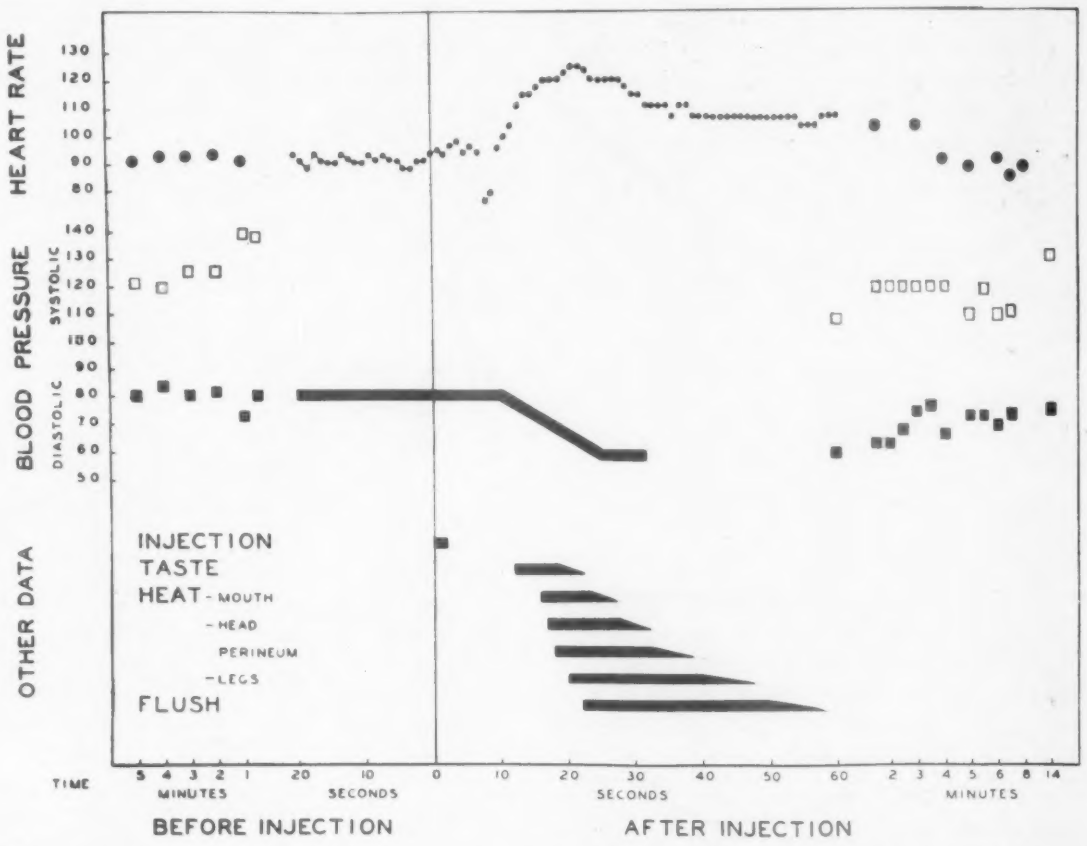


Fig. 12. The usual reaction to the rapid intravenous injection of diodrast. Heart rate calculated from continuous electrocardiogram. Blood pressure determined by the auscultatory method. Observe the interval between injection and reaction, the initial bradycardia followed by tachycardia and fall in blood pressure, and the progressive spread of "heat" through the body. Note the mild and transient nature of the reaction.

(11) The precautions ordinarily used to prevent infection from intravenous injection should be observed. The syringes must be scrupulously clean to prevent sticking of the plungers during rapid injection.

## RESULTS

These results comprise the entire experience with this method including the early trials in which the technique was crude and only one roentgenogram per injection was

injections usually were made after an interval of at least twenty-four hours. Forty-eight injections were for pharmacologic study and 190 for visualization.

Eight injections were primarily for visualization of the superior vena cava, three for the collateral circulation from the arm, and one for the renal blood vessels. All were successful. The pulmonary circulation was outlined 75 times in the 79 injec-

tions made for this purpose. The following structures also were seen: innominate and peripheral veins, 54 times; superior vena cava, 56; right auricle, 65; right ventricle, 67; interventricular septum, 61; pulmonary conus, 63; and pulmonary artery, 62. One or both chambers of the right and the left sides of the heart were visualized 68 times in the 76 injections for cardiac study. The following major divisions were identified: superior vena cava 56 times; right auricle, 57; right ventricle, 64; pulmonary artery, 56; left auricle, 30; left ventricle, 41; and thoracic aorta, 44. Other structures visualized were: peripheral veins, 58 times; auriculo-ventricular groove, 9; tricuspid valve, 1; pulmonic valve cusps, 23; aortic cusps, 12; right ventricular wall, 34; left ventricular wall, 29; interventricular septum, 50; pulmonic sinuses, 35; aortic sinuses, 22; left coronary artery (probably), 1; innominate, left common carotid, and left subclavian arteries, 20; axillary and brachial arteries, 3, and renal vessels twice. The thoracic aorta was visualized 21 times in the twenty-three injections for this purpose. With the present technique it was possible with one injection to visualize the right auricle and ventricle and the pulmonary arterial tree in nearly every case, and the left auricle or ventricle and the thoracic aorta in 80 per cent of the attempts; many of their component parts could also be seen. Less uniform success was obtained in patients with great cardiac enlargement, pulmonary engorgement, mitral stenosis, interventricular septal defect, and auricular fibrillation.

The anatomy of the heart, of the pulmonary circulation, and of the great vessels was demonstrated in normal persons,[40] and abnormalities were observed in heart[41] and lung[47] disease. In 3 patients with stenosis or occlusion of the innominate vein from mediastinal tumor, the site of the lesion and the collateral circulation were demonstrated. The superior vena cava was displaced or distorted by mediastinal neoplasm in 2 patients, by tuberculous adenitis in another, and by a dilated pulmonary artery in a third patient with mitral stenosis. In 2 patients with displacement of the heart due to funnel chest and pulmonary fibrosis respectively, the superior vena cava, the chambers of the heart and the aorta were identified, whereas the heart was completely obscured in the conventional roentgenogram.[48] The normal pulmonary circulation and heart are illustrated in Figures 5 to 8. Figure 5 is the conventional postero-anterior roentgenogram; Figures 6 and 8 are contrast films showing the pulmonary arterial tree and the right chambers in the first one, and the pulmonary veins, the left chambers and the thoracic aorta in the other. The round opacities near each hilum are arteries seen on end and not calcifications. The changes occurring in productive tuberculosis are shown in Figure 10 in which the left branch of the pulmonary artery is elevated and the vascularity of the upper lobes is decreased. Similar changes were observed in the pulmonary fibrosis associated with bronchiectasis and carcinoma of the bronchus, and in hilar adenitis. The pulmonary artery and its branches were differentiated from neoplasm, cysts, calcified nodes, parenchymal calcification and aortic aneurysm at the hilum.

Enlargement of the right ventricle and the pulmonary artery was observed in 3 patients with mitral stenosis, in 4 patients with cor pulmonale, and in 1 patient with interventricular septal defect. The left auricle was enlarged in the first condition but it was normal in size in the other two. Dilatation of the pulmonary veins also was noted in mitral stenosis. The left ventricular cavity was enlarged and the wall thickened in the presence of mitral insufficiency, aortic insufficiency, and arterial hypertension. The changes occurring in severe hypertension are shown in Figure 11 in which the left ventricular wall measured 1.7 cm. Aneurysm of the aorta was demonstrated in 3 patients with syphilis, one of whom had aneurysms of both ascending and descending portions. Diffuse dilatation of this vessel was observed in 6

patients with syphilis, and in 5 others who had both syphilis and hypertension. In one instance, a large aneurysm, previously diagnosed as aortic, was found to involve the pulmonary artery. The dilatation and elongation of the aorta and the striking widening and angulation of the aortic arch found in severe arterial hypertension are shown in Figure 11.

## DISCUSSION

Important practical features of this method are the 70 per cent solution of diodrast, adequate dosage, rapid intravenous injection, accurate determination of the time for exposure, and proper positioning during roentgenography.

The radiopaque substance, diodrast,[32] was used because of the mildness of its pharmacological action observed in animals[6,14,23,38] and man.[42] Skiodan[32] and hippuran[32] were tried, but were found to cause undesirable reactions when injected in effective concentration and amount. Neoiopax[32] was not used because of its reported tendency to cause pain in the arm and shoulder during injection. The 70 per cent solution of diodrast proved the most satisfactory for visualization of the left chambers of the heart and the aorta; lower concentrations, even 40 per cent, were sufficient for outlining the superior vena cava, the right side of the heart, and the pulmonary blood vessels.

Diodrast is the organic iodide compound, 3,5-diiodo-4-pyridone-N-acetic acid and diethanolamine, containing 49.8 per cent iodine. It is not radioactive. Although relatively inert, it causes a prompt fall in blood pressure, tachycardia, respiratory stimulation, an increase in the volume of various organs, and an increase in intestinal tone when injected intravenously in animals.[6,14,23,38] The changes in blood pressure and organs are due to the generalized dilatation of the arterioles and capillaries caused by direct action of the drug. The increase in respiration and intestinal tone were ascribed to direct stimulation of the respiratory center and the intestinal musculature.[14] The mechanism of the tachycardia is not known; in the isolated heart perfusion with diodrast caused an increase in coronary blood flow and amplitude of cardiac contraction, but no change in heart rate.[14] In man, the slow intravenous injection of the drug for urography frequently causes flushing of the face and a sense of warmth; occasionally it is followed by transient nausea and vomiting, erythematous eruptions, respiratory distress and cyanosis—effects which also are produced by similar iodine compounds.[32] A moderate fall in blood pressure results when the substance enters the blood stream more rapidly, as in vasography.[8] The commercial 35 per cent solution causes no detectable injury to the blood vessels or other structures of man[31] or animal[6,14,23,38] when administered in the customary dosage and manner,[32] or even when injected rapidly into artery[6] or vein.[8] There is little or no diffusion of the compound into the erythrocytes or other tissue,[24,46] and it is excreted promptly by the kidney without change.

The *immediate reaction* to diodrast, as it is given in this method, appears ten to twenty seconds after the injection. It consists of a metallic taste, and a wave of intense heat which starts in the mouth and spreads through the body reaching the lower extremities last. Concurrently there is a fall in arterial blood pressure which rarely exceeds 30 mm. Hg, a rise in heart rate of approximately 30 beats per minute, and flushing of the face and the shoulders. Dizziness, weakness, and nausea are observed occasionally. Severe vomiting, sweating, pallor and hypotension occurred in 13 instances, but were relieved promptly by recumbency except in 3 patients who were given epinephrine as well. The reaction is usually over in two to three minutes, although in 5 cases it lasted one-half hour. Transient pain and venospasm at the site of injection occurred in a few instances; but cardiac pain was never produced, not even in the 2 patients who suffered from angina pectoris. Palpitation was experienced rarely; respiratory distress, cyanosis,

and syncope did not occur. The usual reaction to diodrast is shown in Figure 12.

The occurrence of severe reactions led to investigation of diodrast's effect in man, and to search for a suitable antagonist.[42] Continuous electrocardiographic tracings, arterial blood pressure determinations, and clinical observations were made in 23 persons before, during, and after injection; and were repeated in many of this group after therapeutic doses of one or more of the following drugs: sodium amytal, evipal, morphine sulphate, atropine sulphate, ergotamine tartrate, pitressin, and prostigmin. In one case the reaction was studied in both sitting and supine positions. In 4 patients observations were made before and after block of both carotid sinuses to learn the rôle played by the carotid sinus[16,49] in the fall of blood pressure and the cardiac acceleration which occurred regularly, and in the respiratory stimulation and momentary bradycardia observed occasionally. Diodrast (35 per cent solution) was injected into the common carotid artery in 2 instances to investigate its action upon the carotid sinus, the diencephalic centers[7,36] and the cerebral cortex.[22] Intradermal injection of diodrast was made in 25 patients to determine if sensitivity could be detected. To find out if the rapid injection of 60 cc. of liquid would overload the vena cava or the heart,[2] the venous pressure was measured continuously in 3 patients, one of whom had serious heart disease.

These observations in man, although incomplete, indicate that the fall of blood pressure results from the direct dilating effect of diodrast on the small blood vessels, and that the tachycardia may be due to one or more mechanisms: direct stimulation of the sino-auricular node or cardio-accelerator center by the drug; or indirect stimulation of these structures by reflexes initiated in the brain or periphery, or through epinephrine secretion. The carotid sinus is not a factor in the causation of the hypotension and plays little or no part in the tachycardia; it is responsible, however, for the transient bradycardia and the respiratory stimulation. There is no evidence to suggest that the cardiovascular response is caused by direct stimulation of the diencephalic centers or the cerebral cortex, or that the tachycardia results from distention of the right chambers of the heart. The absence of significant change in the electrocardiogram excludes noteworthy effect upon the myocardium, and the normal venous pressure throughout rules out spasm of the vena cava and heart failure from the injection. Posture had no effect upon the reaction in the one patient in whom this problem was studied carefully. Recent observations[30] suggest that the sensation of heat is due to stimulation of nerve endings in the vicinity of the capillary bed by diodrast which has diffused through the capillary wall. Sensitivity to the drug could not be detected by skin test, even in 5 patients who subsequently had severe reactions. No drug completely counteracted the untoward effect of diodrast: amytal, evipal, ergotamine tartrate, pitressin and prostigmin lessened but did not abolish its vasomotor and cardiac effects; morphine and atropine were ineffective, and epinephrine and ephedrine controlled the fall in blood pressure but increased the tachycardia.

*Delayed reactions* occurred infrequently. Urticaria appeared promptly in 15 patients and angioneurotic edema in 2 others; epinephrine gave prompt relief. Dermatitis medicamentosa occurred only once; iodism was never observed. A slight elevation of temperature was observed 9 times; in 2 other patients, a chill and high fever followed injection. Mild thrombophlebitis developed at the site of injection 33 times but was unimportant since it involved only a small segment and caused neither discomfort nor embolism. In 3 of the 5 cases examined several months afterward the vein was patent; and even when the obstruction persisted, the vein above and below it remained open and could be used for injection. In the 5 instances of perivascular infiltration the inflammatory reaction was

mild, thrombophlebitis developed only once, and ulceration did not occur.

No *toxic effect* upon the heart, the lungs, the kidneys, the liver and the blood was discovered although searched for. Clinical and roentgenographic examinations of the heart and the lungs were made repeatedly in more than half of the patients and many were followed in ward or clinic for months. No activation or aggravation of pulmonary disease was detected. Electrocardiograms made in 28 patients showed significant change but once: a man, aged seventy-one, who had had a coronary occlusion previously, developed another thirty hours after injection. Urinalysis in 34 patients, and the dilution and concentration and phenolsulphonphthalein tests in 5 patients disclosed no renal impairment. The bromsulphalein test and the concentration of serum bilirubin and urinary urobilinogen in another 5 patients gave no indication of hepatic disease. The immediate effect upon the blood was investigated carefully in 5 patients and no significant change was detected. In a larger series, comparison of the routine blood examinations made before and for weeks after injection revealed no evidence of injury to the hemopoietic system.

In summary, diodrast, is a suitable radiopaque medium since it is freely miscible with the blood, rapidly eliminated, relatively nontoxic and inert, and nonirritating except at the site of injection in a few patients.

Visualization of the cardiovascular structures in the thorax requires adequate dosage and rapidity of injection of the contrast substance. The dose must be sufficient to make opaque enough blood to fill the right chambers of the heart and the pulmonary circulation at the same time and, later on, the left chambers of the heart and the thoracic aorta. The delivery of diodrast into the vena cava must be fast enough to produce a high degree of radiopacity in the blood entering the heart so that there may be an effective concentration after passage through the heart and the lungs. The minimal effective concentration of diodrast, calculated from the work of Lopo de Carvalho and Egas Moniz[26] would be approximately 3.4 per cent which would permit a twenty-fold dilution of the injected solution. Rapidity of injection is achieved by the use of large bore apparatus, Luer-Lok connections, large vein, elevation of the arm, and simultaneous inspiration. Prompt arrival in the vena cava is insured by the forcible flushing of the peripheral veins with the blood which overlies the diodrast in the syringe. Delay in passage through the pulmonary circulation due to the involuntary increase of intrathoracic pressure, which tends to occur during maintenance of the inspiratory position, is prevented by the passive exhalation which follows injection.

The roentgenograms must be made at the proper moment and in the best position for each structure. Since the intervals between injection and opacification of the right side of the heart and the pulmonary circulation are short and nearly uniform, standard intervals can be used successfully in the average patient.* In the exceptional case, the interval can be learned before injection from the ether circulation time to the lungs. In 7 patients the ether circulation time averaged five seconds, whereas the time required for the opaque medium to reach the pulmonary arterial tree was 3.3 seconds. The cyanide method was used to determine the circulation time to the thoracic aorta, although other methods[12,13,51] would probably be satisfactory. To insure accuracy, enough cyanide must be given to produce a conspicuous stimulation of respiration having an abrupt onset, for the onset indicates the time of arrival in the carotid sinus and also in the descending aorta. Frequently both the left chambers and the thoracic aorta are made opaque at this time due to the stringing out of diodrast in its passage through the heart and the lungs. Maximal opacification of the left side of the heart, however, is attained a second or two earlier.

The sitting position was used routinely.

* See footnote page 6.

Neither prone nor supine position was suitable, as the need for elevation of the arm excluded the first one, and poor roentgenographic results the other. The posteroanterior position of the chest provides an excellent view of the superior vena cava, the lung roots, and the pulmonary blood vessels, but it gives an unsatisfactory picture of the heart and the aorta because they lie obliquely in the thorax and thus are seen from an angle. For accurate study, the heart must be looked at directly from its apex or side.[35,45] The apical view is obtained by use of the left anterior oblique position in which the apex is pointed toward the film, the two ventricles lie side by side, and the aorta crosses in lateral view. This position is suitable for study of the cavities and walls of both ventricles, the interventricular septum, the left branch of the pulmonary artery, the pulmonic and aortic valves and the entire thoracic aorta. The right anterior oblique position gives a lateral view of the heart in which the ventricles lie anteriorly with the auricles behind, the pulmonary artery is more in profile than in the left position, and the aortic arch appears on edge. The auricles, the auriculo-ventricular groove, the inflow and outflow portions of the right ventricle, the tricuspid and mitral valves, and the right branch of the pulmonary artery were viewed best in this position. The superior vena cava can be outlined in posteroanterior, lateral and oblique positions.

Experience has shown that this method is safe. Although it is generally true that rapid intravenous injection is dangerous,[19] clinical trial showed that the 70 per cent solution of diodrast could be given in this way without serious ill effect. The immediate reaction usually was mild, and severe reactions, when they occurred, were transient. Delayed effects were unimportant. Pulmonary embolism from blood clot formed in the apparatus was not observed, probably because the frequent flushing with normal salt solution prevents clotting in the needle and the stopcock, and the diodrast prevents it in the syringe. In 2 instances blood from the syringe failed to clot after fifteen minutes and two hours, respectively, although the bleeding and clotting times were unaffected in the 5 patients in whom blood studies were made before and after injection. The absence of fatality and noteworthy injury is final proof that the method is harmless.

The procedure is no more difficult to perform than many diagnostic tests, and it can be carried out in both ambulatory and bed patients. No aftertreatment is required. The usual roentgenographic and laboratory apparatus is used with little or no modification. The technique of injection is relatively simple requiring, however, more skill than is ordinarily needed for venipuncture and injection. The discomfort experienced by the patient is usually moderate, comparable to that caused by gastric lavage, bronchography and spinal puncture. Two patients actually liked the test: one, a man aged seventy-four, with syphilitic aortitis, found the reaction "pleasantly warm"; the other, a boy of nineteen, described it as "an exquisite sensation." The reaction to diodrast, whether mild or severe, does not interfere with visualization since it invariably occurs after the roentgenograms have been made.

Certain obvious technical improvements can be made. Synchronization of heart beat and exposure[18] would permit the roentgenograms to be made during the diastolic pause or at other points in the cardiac cycle, and thereby make possible accurate observation and mensuration. By using cineroentgenography[48] or rapid, serial roentgenography, it should be possible with one injection to visualize all the important divisions of the heart and of the thoracic blood vessels to be seen in the position used. By making serial roentgenograms simultaneously[34] in the frontal and lateral positions or in the two oblique positions, each region could be visualized in two planes and from this three-dimensional study volumetric determinations[21] could be made. Of practical importance, a

complete study of the heart could then be made with one injection. Roentgen kymography[17] during opacification should give a graphic record of the movement of both surfaces of the cardiac and the vascular walls, information not obtainable by ordinary visualization or roentgen kymography. Simplification of the technique of injection by dispensing with the respiratory maneuvers and the flushing in of diodrast with blood may be feasible. Finally it is possible that the undesirable side-effects can be eliminated by developing a more inert radiopaque compound or by finding a better antagonist. Larger doses then could be given and greater radiopacity produced.

Clinical experience has proved this method to be of value in the diagnosis of heart and lung disease. In both fields it frequently was possible to establish diagnoses which formerly were based upon less direct evidence. At the present time the chief value in pulmonary disease is twofold: the recognition of abnormalities of the mediastinal and the hilar blood vessels whether due to intrinsic disease or to distortion or displacement from without, and the differentiation of these blood vessels from adjacent structures such as mediastinal neoplasm hilar adenitis, pulmonary cyst and calcification. Less striking results are obtained in disease of the pulmonary parenchyma. Decreased vascularity was demonstrated in pulmonary emphysema and the localized fribrosis due to tuberculosis and suppurative disease, but this method gave no assistance in the diagnosis of tuberculous cavitation, lung abscess, and neoplasm. It is possible that characteristic deviations from the normal vascular pattern of the lung can be worked out for pulmonary disease.

In heart disease visualization permits a precision in diagnosis previously impossible. No longer must roentgenographic evidence of disease depend upon change in the silhouette of the entire heart or the distortion of adjacent structures. Instead, each chamber and great vessel can be visualized separately, and the nature and degree of abnormality ascertained. Exact mensuration of the heart thus becomes a possibility. At the same time, the circulation time of the blood to the various parts of the cardiovascular system can be determined objectively. Characteristic changes were observed in congenital, rheumatic, pulmonary, hypertensive, and syphilitic heart disease. Diagnosis was made possible in 3 patients with cor pulmonale and another with syphilitic aneurysm of the pulmonary artery. In a third patient with syphilis, hypertension, and widening of the aortic arch, dilatation of the aorta was excluded. This method promises to be of practical value in the differential diagnosis of heart disease, the recognition of early organic change, and the exclusion of heart disease in the normal.

## SUMMARY

Visualization of the heart and the thoracic blood vessels is a practical procedure. The method consists of the rapid injection of 25 to 45 cc. of a 70 per cent solution of diodrast into an arm vein, and the making of roentgenograms when the chambers of the heart and the blood vessels are opaque to the roentgen ray. The interval between injection and exposure depends upon the region to be visualized. Average intervals can be used for the right side of the heart but the circulation time to the left chambers and the aorta should be determined. The frontal position is used for study of the pulmonary circulation, the oblique positions for the heart and the aorta. The organic iodide compound, diodrast, has negligible toxicity and is rapidly excreted by the kidneys. Its pharmacological effects are usually mild, and it is nonirritating except at the site of injection in a small proportion of cases. Two hundred and thirty-eight injections were made without serious ill effect.

This method provides information regarding the anatomy and the physiology of the normal and diseased cardiovascular system heretofore unobtainable. It is possible to determine the site of stenosis or

occlusion of the superior vena cava and its tributaries, and the course and extent of the collateral circulation. The vascular nature of the hilum may be demonstrated and these vessels differentiated from adjacent structures. Accurate study of the arterial and venous patterns of the lung can be made. The internal structure of the living heart has been revealed for the first time and abnormalities due to disease have been observed. The following structures became visible: the superior vena cava and its tributaries, the four chambers of the heart, the ventricular walls and the interventricular septum, the tricuspid, pulmonic and aortic valves, the pulmonic and aortic sinuses, the pulmonary artery, and the entire thoracic aorta including its wall and the branches from the arch.

## CONCLUSIONS

(1) Visualization of the chambers of the heart, the pulmonary circulation, and the great vessels in man is safe and practical.

(2) This procedure gives exact information regarding these structures which has heretofore been unobtainable.

(3) It opens up a new field for the study of the anatomy and the physiology of the circulation.

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# VENTRICULOGRAPHY OF THE FOURTH VENTRICLE*

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DURING the period 1927 to 1937, 3,381 ventriculographies and encephalographies were performed at the Seraphimer Hospital. The cases (Table 1) were from the Neurosurgical Clinic (Chief, Prof. Olivecrona) and the Neurological Clinic (Chief, Prof. Antoni).

Special apparatus was used for the roentgen examinations. The target-film distance was constant in every position, the tube moving in a hemisphere about the patient's head. Exposures were made at 90 kv. (peak) and 20 ma., delivered through a 1.5 kw. tube, the time varying from ½ to 1 second. At first the secondary diaphragm consisted of a stationary Lysholm grid. During the last year a Lysholm all-metal grid was used. This technique allowed adequate exposure, yet avoided excessive contrast. Our purpose is not to obtain films of good contrast, as we find that the detail of the air shadows is difficult to determine. With the harder or flatter, well-exposed film, the margins of the smaller collections of air such as those in the aqueduct, fourth ventricle and cisterns are better defined. There is less chance both of misinterpretation and of overlooking important details.

During the past five years our method of localizing air bubbles has been to use two non-stereoscopic films made in different planes, with the position of the patient's head unchanged between the two exposures. This procedure proved to be more reliable and less difficult than our former technique employing stereoscopy.

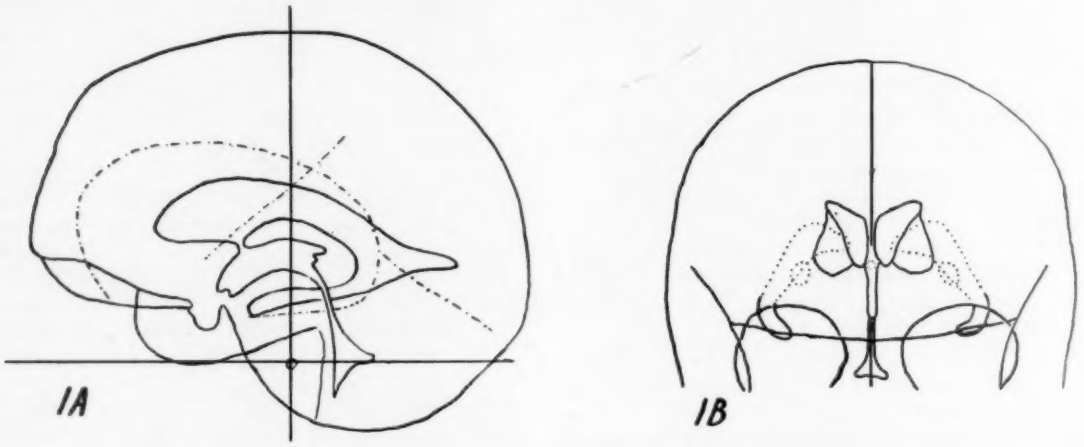


FIG. 1. Reconstruction of the normal ventriculogram from roentgenograms. *A*, lateral view; *B*, anteroposterior view.

As all roentgenograms were made with identical target-film distance, it has been possible to combine in composite drawings the portions of the ventricles seen in the various films (Fig. 1).

Drawings of the ventriculographic findings in 400 cases in which clinical examination and subsequent developments proved the absence of tumor indicate that the size and shape of the normal ventricles are fairly uniform. Very small lesions and variations are more easily detected when this drawing of normals is used as a standard for comparison.

We have found in examining tumors located below as well as above the ten-

* From the Roentgen Department of the Seraphimer Hospital, Stockholm. Read at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13–17, 1937. Translated by Frederic E. Templeton, M.D., Chicago.

torium that a gaseous contrast medium gives better results than do the iodized oils or thorotrast. Prior to 1936, 102 cases of suspected infratentorial tumors were examined with either lipiodol or thorotrast. Since 1936 the method has been discarded in favor of air injection, as the positive contrast media were harmful to the patients. With improved technique and with greater experience in interpretation, the results with air injection using the Dandy technique are comparable to those obtained with the iodized oils. To ensure successful examination a sufficient quantity of air of approximately half the volume of the lateral ventricles must be introduced. In practice, the air column, as seen in the lateral view taken with the ray parallel with the floor, should reach a height of at least 3 to 4 cm. This must be determined by preliminary roentgenograms. Cases in which only a small volume of air was introduced necessitated the taking of a greater number of films in order to obtain a complete reconstruction.

Table I

A summary of all the cases examined by contrast media, from 1925 to 1936

| | Lipiodol | | Arteriography | |
|---|---|---|---|---|
| | Air | Thoro-trast | a. carotis | a. vertebr. |
| 1925–1929 | 105 | 2 | — | — |
| 1930 | 52 | — | — | — |
| 1931 | 132 | — | — | — |
| 1932 | 308 | 12 | 11 | — |
| 1933 | 358 | 54 | 26 | — |
| 1934 | 582 | 42 | 29 | — |
| 1935 | 741 | 13 | 63 | 1 |
| 1936 | 1007 | — | 61 | 4 |
| Total | 3285 | 123 | 190 | 5 |

The roentgen technique and the procedure followed at the examination are described in our publication "Das Ventrikulogram." In general, frontal and lateral films are supplemented by semi-axial views. By visualization of the ventricular system from the front, from the side and obliquely from above, a clear three-dimensional conception of the topography of the ventricular system is obtained.

Filling the fourth ventricle with air requires special maneuvers. These, best learned with the aid of a model of the ventricular system and by earnest practice on clinical cases, are carried out as follows: The patient is first placed on his left side so that the greater part of the air collects in the anterior horn of the right ventricle. The head is then rotated to allow the air to pass through the foramen of Monro into the third ventricle. This is accomplished by mild shaking of the head. Rotation is continued until the forehead rests against the examining table. Three exposures are made in rapid succession, the patient's position remaining unchanged. The first view is in the frontal projection, with the tube set at 90° to the film; the second, a semi-axial view with the tube angled 30° toward the feet; the third, a lateral view, with the ray parallel to the floor. These exposures completed, the rotation of the head is continued, thus enabling the air to collect in the left lateral ventricle. The head is then rotated in the opposite direction until the right side is uppermost; the main part of the air collects in the lateral ventricle but some passes through the foramen of Monro to the fourth ventricle. A lateral

Fig. 2. Position of the patient's head used to facilitate free flow of fluid and air out of and into the ventricular system.

### Table II

A CLASSIFICATION OF TUMORS ABOVE THE TENTORIUM, BASED ON 398 VERIFIED TUMORS

A. SUPERIOR CEREBRAL TUMORS WITHOUT DISPLACEMENT OF THE TEMPORAL HORN
- I. Medial or parasagittal
  - a. Anterofrontal
  - b. Upper frontal
  - c. Frontoparietal
  - d. Parietal
  - e. Occipital
- II. Lateral
  - a. Parietal and some in the fissure of Sylvius
  - b. Frontal
  - c. Occipital

B. CEREBRAL TUMORS WITH DISPLACEMENT OF THE TEMPORAL HORN
- a. Certain tumors in the fissure of Sylvius
- b. Posterotemporal
- c. Anterotemporal

C. BASAL TUMORS WITHOUT DISPLACEMENT OF THE TEMPORAL HORN
- a. Subfrontal
- b. Supra- and intrasellar

D. BASAL TUMORS WITH DISPLACEMENT OF THE TEMPORAL HORN

E. CENTRAL TUMORS

F. INTRAVENTRICULAR TUMORS

G. TUMORS FROM SEPTUM PELLUCIDUM AND CORPUS CALLOSUM

### Table III

TUMORS OF THE BRAIN STEM AND BENEATH THE TENTORIUM

| | |
|---|---|
| 1. Anterior part of the third ventricle and foramen of Monro | 12 |
| 2. Posterior part of the third ventricle | 33 |
| 3. Lamina quadrigemina | 12 |
| 3. Stenosis of the aqueduct | 13 |
| 5. Pons | 8 |
| 6. Cerebellopontine angle* | 6 |
| 7. Roof of the fourth ventricle above fastigium | 26 |
| 8. Cerebellar hemisphere | 39 |
| 9. Floor and roof of the fourth ventricle below fastigium | 26 |
| 10. Intraventricular tumors (fourth) | 10 |
| 11. Arachnoiditis in the posterior cranial fossa | 23 |
| Meningioma from tentorium | 1 |
| Meningioma from clivus | 3 |
| Total Number of Verified Tumors | 212 |

* Acoustic tumors diagnosed without ventriculography during the period 1934–1936. An expansion deformity of the internal meatus was present in 90 per cent of 39 cases.

roentgenogram is then taken. The head is now slightly lowered and turned so that the left side is uppermost and another lateral roentgenogram is taken. If the mastoid processes are large and aerated, an oblique film is made in order to free the shadow of the fourth ventricle from that of the mastoid cells. The films are then developed and studied. If the fourth ventricle fails to properly visualize the procedure is repeated.

In order to release an air lock, the patient's head is lowered and rotated to the position shown in Figure 2, and then gently shaken. In this position the fastigium is uppermost.

Success in visualizing the fourth ventricle depends upon repeated attempts to coax air into the ventricle by manipulation of the head, the breaking up of air-locks and the immediate taking of films to show the air as it passes through the fourth ventricle into the subarachnoid space. The same degree of diligence must be used to obtain satisfactory films of the fourth ventricle as is used in searching for a duodenal ulcer. A fixed routine procedure often fails to yield results.

Using ventriculographic localization, we have divided brain tumors into various groups (Tables II and III).

Diagnosis of a tumor in the posterior part of the third ventricle is not difficult. It is more difficult to determine its operability. Benign pinealomas give a well-defined filling defect with more or less complete filling of the suprapineal recess. If air surrounds the tumor on both sides. if the outline is smooth and calcification is present, the tumor is probably operable (Fig. 3). Calcification alone, however, does not always signify a pinealoma. In our series four such tumors with calcification proved to be gliomata and one a tuberculoma. If, on the other hand, there is firm attachment on one side to the thalamus, as often happens, so that air can only surround one side of the tumor, it is probably inoperable (Fig. 4). A source of difficulty occurs when an operable tumor of the posterior part of the third ventricle is pushed downwards below the incisura tentorii. This may be mistaken for an inoperable tumor of the corpora quadrigemina.

If the ventricular defect is small in comparison with the degree of displacement of the aqueduct, the tumor is likely to be quadrigeminal. Careful examination of the aqueduct gives valuable information. Quadrigeminal tumors displace the duct

Fig. 3. Operable calcified tumor in the posterior part of the third ventricle.

towards the clivus but not laterally (Fig. 5).

Tumors involving the upper portions of the vermis may compress or completely occlude the aqueduct (Fig. 6). In early cases there is basilar displacement of the infratentorial part of the aqueduct. This is very often associated with a dorsal kinking of the smaller supratentorial part of the duct. In the larger tumors the adjacent portions of the fourth ventricle are also displaced downwards. It is this downward displacement of the aqueduct that helps to differentiate tumors of the vermis from stenosis of the aqueduct. In all the cases of tumors of the vermis which we have examined, the aqueduct has been found to lie in the midline when viewed in the frontal projection. Occasionally the aqueduct is blocked by a pure stenosis. This may be caused by a gliosis around the duct or to some inflammatory process. The narrowing is usually found about 1 cm. from the third ventricle and in our cases has

Fig. 5. Tumor of corpora quadrigemina displacing aqueduct downwards. Arrow indicates aqueduct.

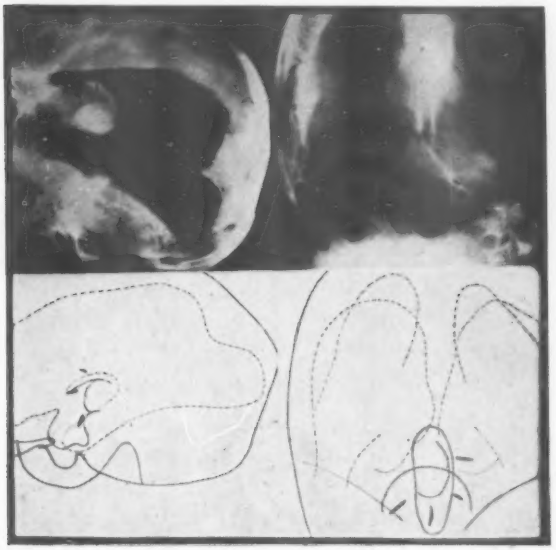

Fig. 4. Inoperable tumor in the posterior part of the third ventricle. Note attachment to thalamus in frontal view.

Fig. 6. Upper vermis tumor. Note kinked basilar displacement and blocking of the aqueduct.

FIG. 7. Aqueduct stenosis, Type I. Note conical blocking without displacement of aqueduct.

been one of two types. In the first type the upper part of the duct presents a conical appearance (Fig. 7). In such cases we have not been able to fill the fourth ventricle and have concluded that the stenosis is probably complete. The second type shows a dumbbell-shaped defect (Fig. 8). In these cases in which we are able to fill the fourth ventricle there is obviously an incomplete stenosis.

In tumors of the cerebellar hemispheres the ventriculographic findings vary with the extent and location of the tumor. In tumors of the superior portions of the hemispheres, the findings are similar to those described for the upper portions of the vermis. The supratentorial part of the aqueduct shows the dorsal kink and the infratentorial part shows basilar displacement, but in these cases there is lateral displacement combined with basilar bowing (Fig. 9). The degree of basilar bowing naturally becomes greater the nearer the tumor approaches the midline. We have succeeded in filling the fourth ventricle in all of our cases so have concluded that complete blockage of the aqueduct from pure cerebellar hemisphere tumors must be relatively rare.

Tumors of the vermis located beneath the fastigium press the fourth ventricle forwards and upwards. The ventricle is

FIG. 8. Aqueduct stenosis, Type II. Note the dumbbell-shaped defect of the aqueduct.

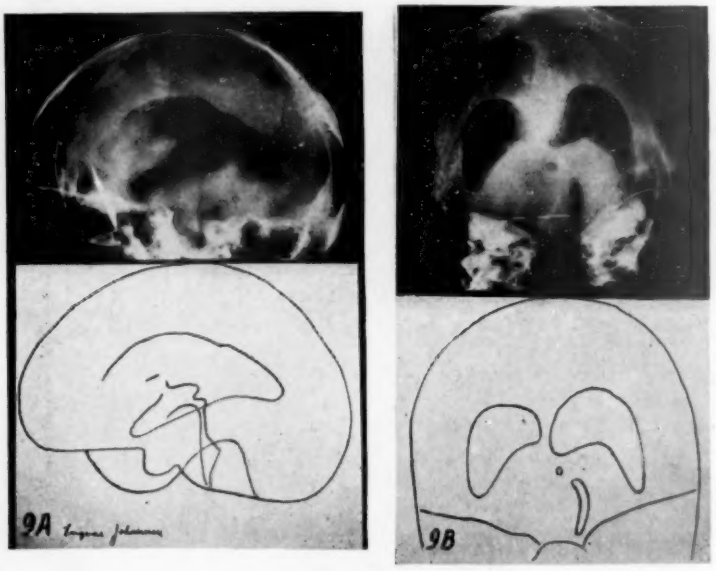


FIG. 9. *A*, left-sided cerebellar tumor, oblique view. Note kinking of the aqueduct and forward displacement of the fourth ventricle. *B*, same tumor, frontal half-axial view. Note lateral displacement of aqueduct and fourth ventricle. The tumor is high up in the left cerebellar hemisphere.

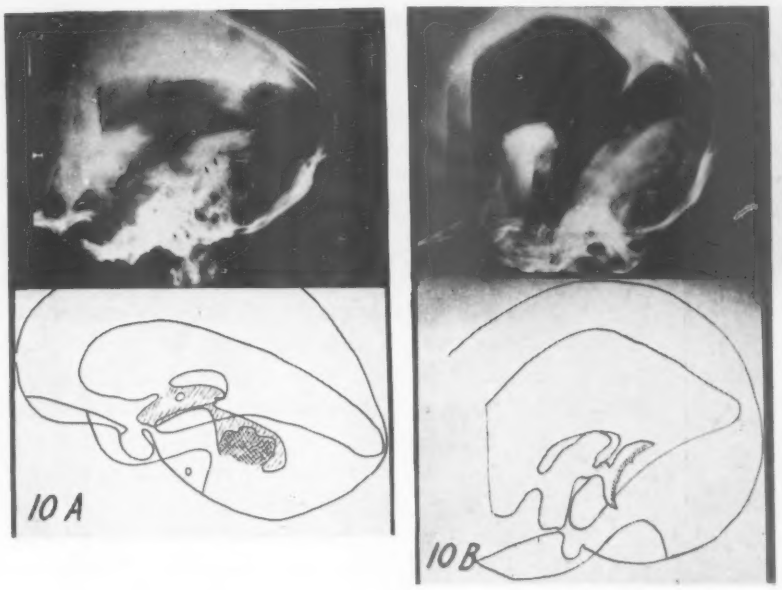


FIG. 10. *A*, papilloma. Note irregular filling defect in the fourth ventricle. *B*, medulloblastoma. Note short, wide aqueduct and smooth filling defect.

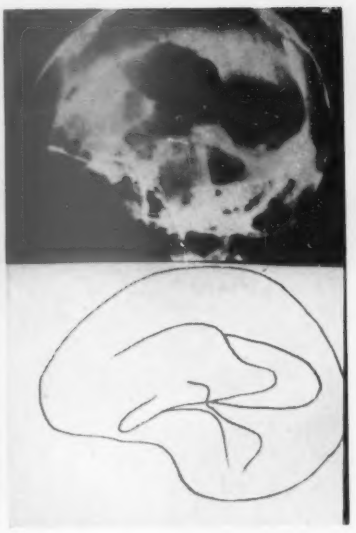

FIG. 11. Pontine tumor. Note dorsal displacement of aqueduct.

usually enlarged and the aqueduct dilated. Supratentorial displacement is slight or entirely absent. Large tumors involving the floor of the fourth ventricle or the infraventricular regions cannot be differentiated roentgenologically from tumors of the lower vermis. On the other hand, when the tumors are small and do not fill or collapse the ventricle, they can be outlined against the surrounding air. If the tumor surface is irregular, the most probable diagnosis is papilloma; if smooth, medulloblastoma or ependymoma (Fig. 10).

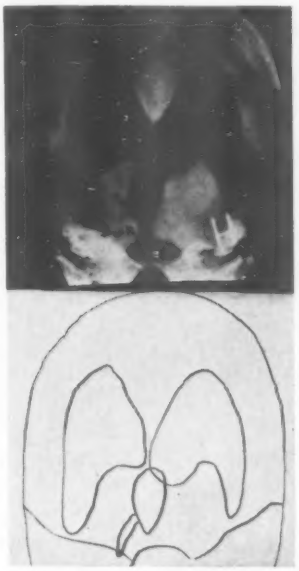

FIG. 12. Cerebellopontine angle tumor. Frontal half-axial view showing lateral displacement of aqueduct. In a lateral view there is dorsal displacement only.

FIG. 13. Arachnoiditis, Type I.

Tumors of the pons and cerebellopontine

angle present similar findings in the lateral views. The fourth ventricle and aqueduct are displaced posteriorly, this displacement causing the aqueduct to show posterior bowing. In cases of pontine tumors frontal views show the aqueduct and fourth ventricle lying in the midline but in cerebellopontine angle tumors these structures are displaced laterally (Fig. 11). Cerebellopontine angle tumors may also indent one of the lateral portions of the fourth ventricle. Pontine tumors are often associated with only a mild degree of hydrocephalus and in some cases there may be dilatation of the ventricular system (Fig. 12).

FIG. 14. Clivus meningioma. Note dorsal displacement and flattening of floor of fourth ventricle.

Two types of posterior cisternal arachnoiditis are distinguishable. One, caused by occlusion of the foramina of Luschka and Magendie, produces a symmetrical hydrocephalus and is relatively easy to diagnose (Fig. 13). The other results in the formation of cysts and cannot be differentiated roentgenologically from other expansile processes.

In 2 cases of meningioma arising from the region of the clivus we have observed dorsal displacement of the aqueduct and flattening of the floor of the fourth ventricle whereby its shape has become altered. In a recent third case we were able to diagnose a clivus meningioma before operation (Fig. 14).

The only meningioma of the tentorium we have observed gave the picture of a cerebellar hemisphere tumor, but as the occipital horn also was displaced we were able to diagnose a dumbbell-shaped meningioma.

## SUMMARY

1. A technique for the demonstration of tumors involving the brain stem is presented.

2. The roentgenologic criteria for recognizing tumors of the brain stem are described.

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# ROENTGEN DIAGNOSIS AND TREATMENT OF ANGIOMA OF THE TYMPANIC CAVITY*

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THIS paper deals with those angiomata which occur in that portion of the auditory organ internal to the tympanic membrane. Many of such tumors extend into the external auditory canal and can easily be confused with those originating external to the drum. The latter, however, are not included in this study.

Two cases are herewith presented.

CASE 1. B. M. (11020, service of Dr. W. J. Mixter), aged thirty-nine when first seen in August, 1933. In 1918, following influenza, this patient had an acute otitis media of the right ear. About 1930 he began to have severe right-sided headaches with pain and tenderness in the right ear. After about one year there was sudden discharge of yellow pus, lasting about ten days, followed by slight deafness on that side. His right eye became swollen and he had double vision on several occasions. The symptoms gradually decreased so that by eight months before admission he was free of them. However, two months later the disturbances recurred, associated with occasional slight nausea, blurring of vision, dizziness, staggering in the dark, harshness of the voice with difficulty in speaking, and twitching of the muscles of the right side of the face. Neurological examination indicated involvement of the right seventh cranial nerve and probably also the fifth, sixth, eighth, tenth and twelfth. A polypoid mass was found completely occluding the external auditory canal. Roentgenograms showed enlargement of the right external auditory canal, erosion of the petrous pyramid and widening of the internal auditory canal. The mastoid emissary foramen and groove of the emissary vein were markedly enlarged. No abnormality was present on the left side (see Figs. 1 to 5). A biopsy taken from the mass in the external auditory canal was reported hemangioma.

It was considered that the lesion was not suitably situated for surgical exposure and an operation was not performed. Roentgen therapy has been the sole form of treatment.

The first series consisted of four treatments of 200 r each (measured in air), given in daily intervals with 200 kv. (peak), filtration of 0.5 mm. copper and 1.0 mm. aluminum, at 60 cm. distance. The field of 10 by 10 cm. was centered over the right external auditory meatus and directed to include the tip of the petrous portion of the temporal bone. When seen ten weeks later there had been definite improvement. Diplopia, headache, dizziness and nausea had been completely relieved, and though the voice was still harsh, speech was much less difficult; muscular twitching was still present. The growth in the external canal had decreased considerably in size.

At this time a second series was given, the distance being increased to 70 cm. A 5 cm. cone was used, 600 r was administered to the right ear as before and in addition 400 r through the left base, cross-firing. At the end of six months the tumor in the external canal was no longer visible and the patient was showing slight further improvement; the muscular twitchings were still present. Consequently a third course of therapy was administered, cross-firing from all directions through a small cone until 2,000 r had been given (April, 1934). Further treatment was carried out during October and November, a total of 3,000 r through 10 by 10 cm. fields, directed towards the right ear from numerous directions. The only complaint at this time was slight hoarseness of the voice.

A year later, severe headaches having returned with an increase in neurological findings, 2,100 r was given in the same manner as before. In November, 1936, he was complaining of occipital headaches and tinnitus; 1,100 r was given. In March, 1937, he was having diffuse right-sided headache and feeling much worse; 1,800 r was administered. In May slight headache was still present but the facial muscles had improved.

In the hope of preserving skin and hair no field had received more than 800 r during any one series of treatments. Although each series of treatments has produced an epilation, the

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hair has remained satisfactory except for an epilated margin of 1 cm. along the hair line just behind the right ear.

The skin is somewhat dry but there is no telangiectasis. We expect to continue treatments when indicated but surgery will probably be necessary for complete relief.

CASE II (U 10744, service Dr. J. S. Hodgson). This patient, aged thirty-one, was admitted in January, 1937, complaining of severe occipital headaches which had been present for four months. For three months there had been nausea with occasional vomiting as well as difficulty in walking and in maintaining her balance. All symptoms had become progressively worse. Neurological examination showed involvement of the left fifth, sixth, seventh, eighth and twelfth cranial nerves and possibly the spinothalamic tract in the medulla. Roentgenograms showed increased size of the vascular channels of the left side of the skull and enlargement of the foramen and groove for the left mastoid emissary vein. The external auditory meatus was enlarged and there was erosion of the petrous pyramid and widening of the internal auditory canal. Some destruction of the mastoid cells was present. No abnormality was seen on the right side (see Fig. 6). Inquiry revealed that the patient had for years been deaf in the left ear and tinnitus had been present. Ten years previously a hemangioma of the left ear had been removed, its presence at that time having been made evident to her by an acute hemorrhage from the ear. On examination of the left ear there was found "an

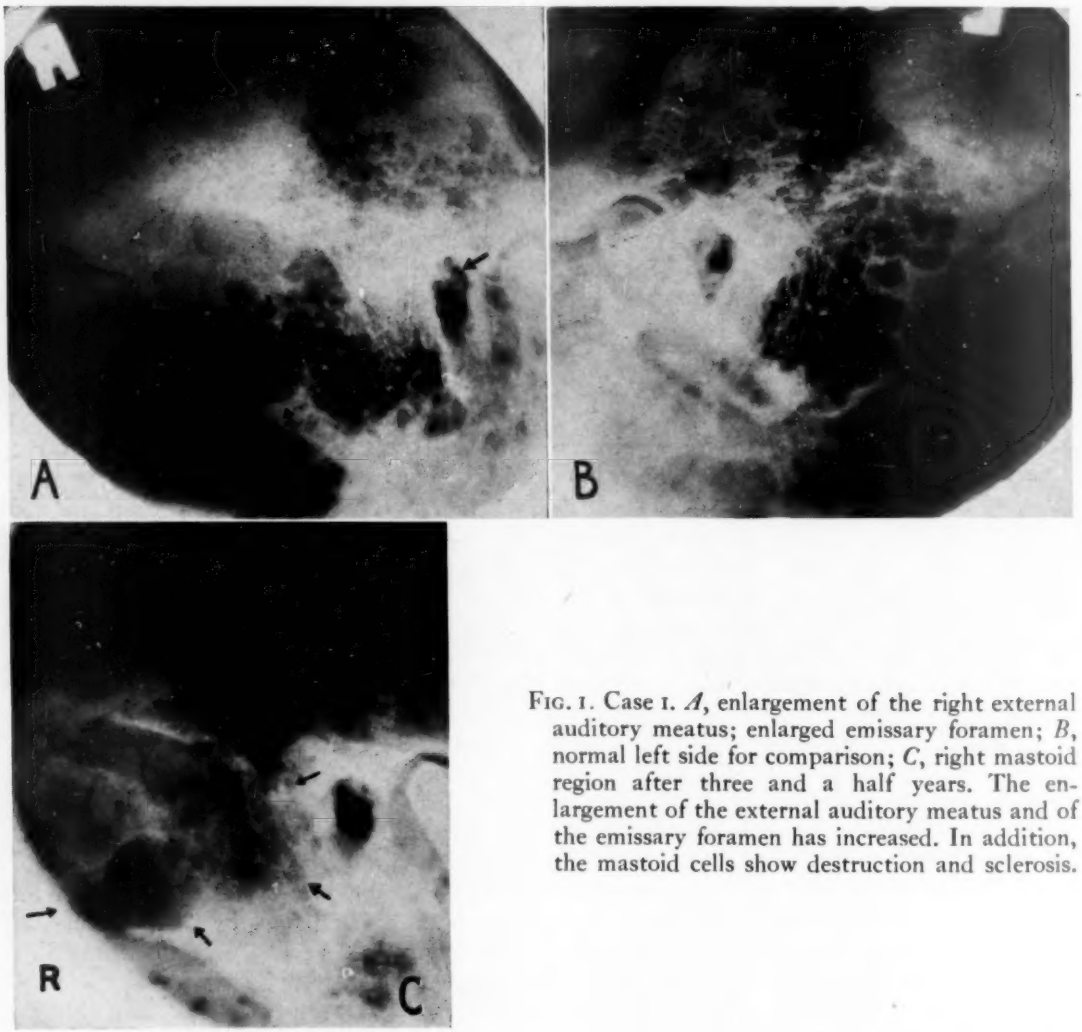


FIG. 1. Case I. *A*, enlargement of the right external auditory meatus; enlarged emissary foramen; *B*, normal left side for comparison; *C*, right mastoid region after three and a half years. The enlargement of the external auditory meatus and of the emissary foramen has increased. In addition, the mastoid cells show destruction and sclerosis.

appearance suggesting a hemangioma behind the drum." Incision of the drum produced considerable bleeding. A biopsy taken from the middle ear was reported hemangioma.

In view of the response to roentgen therapy shown by Case 1, this form of treatment was carried out and no operation was performed. The first course consisted of 1,200 r to the left ear and mastoid region through 6 by 8 cm. portals in daily doses of 200 r, the distance being 50 cm. with 200 kv. (peak), filtration 0.5 mm. copper and 1.0 mm. aluminum. The second series was given six weeks later at which time no improvement had been noted; smaller portals (4 by 5 cm.) were used; the lesion was irradiated from all directions by cross-firing, and a total of 1,900 r was given. When the patient returned for further treatment in June, 1937, she was definitely worse and on consultation with her physician it was decided to do a subtentorial exploration. The exploration was unsuccessful because of extreme intracranial pressure. The region of the suspected disease could not be examined. There has been no further treatment or follow-up visits.

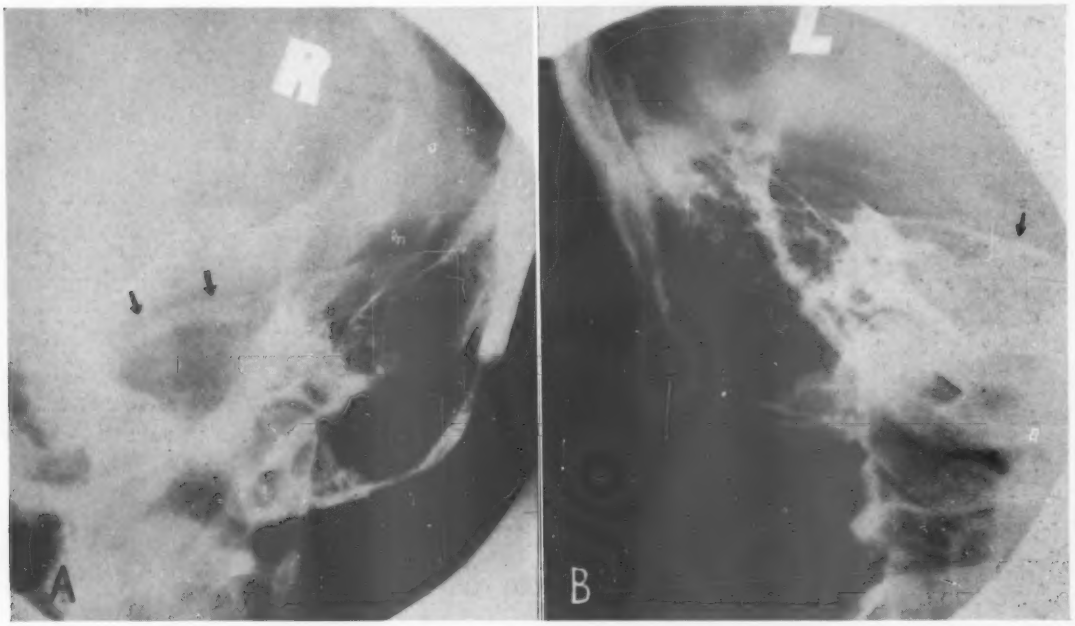


Fig. 2. Case 1. Stenvers projection. *A*, destruction of right petrous pyramid; *B*, normal left side for comparison.

Angiomata, primary in the tympanic cavity, are of rare occurrence; only a few references to this condition are to be found in the literature. Furstenberg[12] found only one such case in 40,000 admissions to the Department of Otolaryngology at the University of Michigan. There is no predilection for any particular age group; the ages in the cases recorded in the literature have ranged between three years and seventy-six years. The most common complaint is pain, usually in the region of the ear, but sometimes in the mastoid region as well as the face and head, and even radiating to the shoulder. Deafness, dizziness, tinnitus and throbbing are mentioned by many of the patients. Paralysis of the facial nerve is of frequent occurrence. Involvement of other cranial nerves may be observed and even signs of increased intracranial pressure. A history of chronic discharge from the ear is common, bloody as a rule, and bleeding, usually profuse, is almost invariably produced by attempts at removal.

The growth is more frequently observed as a fleshy dark red or bluish smooth polyp, sometimes pulsating, presenting in and usually obstructing the external canal. It

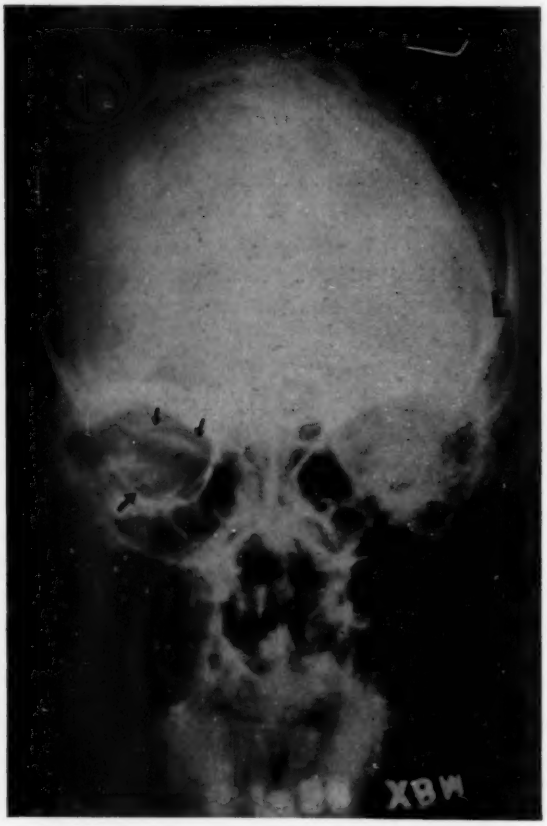


FIG. 3. Case 1. Dorsofrontal projection showing erosion of right petrous pyramid and internal auditory canal.

originates in most cases in the middle ear but in some instances it arises from the tympanic membrane and extends into the middle ear. As pointed out by Thorell,[19] these tumors have markedly invasive qualities, not only eroding the external meatus but also extending inwards. Thus mastoid involvement is frequent, though sometimes at operation this region may be found free from disease. Death may occur due to its growth and destructive properties[2,5] but metastases are rare; in one case,[3] histologically proved to be malignant, there was extension of the neoplasm to the glands of the same side of the neck with ultimate death; in another[6] (endothelioma) there occurred multiple peritoneal metastases. The lesions are of such infrequent occurrence that no uniform nomenclature has been generally adopted. As pointed out by Ewing[8] there is much controversy over the classification of endotheliomata, hemangiomata and lymphangiomata. Consequently the terminology varies and while some have used the term "polyp," other writers have designated them as hemangio-endothelioma, angiosarcoma, etc.

The diagnosis in the cases reported in the literature has been made entirely by means of the clinical evidence and biopsy. Although Newhart[16] (discussing primary carcinoma of the middle ear) in 1917 stated that "roentgenography of the mastoid region offers large future possibilities as an aid to diagnosis by the recognition of the destruction of bone before the growth has extended beyond the tympanic cavity," the earliest reference to the changes shown by roentgen examination in these angiomatous tumors is that of Richman[17] in 1928. In his case "the temporal bone showed highly irregular pneumatization and slightly forward location of the lateral sinus." Fowler[10] in 1931 found "a four plus shadow within the mastoid cells and absorbed areas throughout the lower half of the mastoid process." Bergara and Bergara[2] (1933) observed extensive bone destruction in the region of the ear. Schall[18] (1935) pointed out that in the early stages roentgen examination may be of no diagnostic value; in 1 of his 2 cases while roentgen rays revealed nothing abnormal, extension of the tumor to the deep posterior canal cells was found at operation.

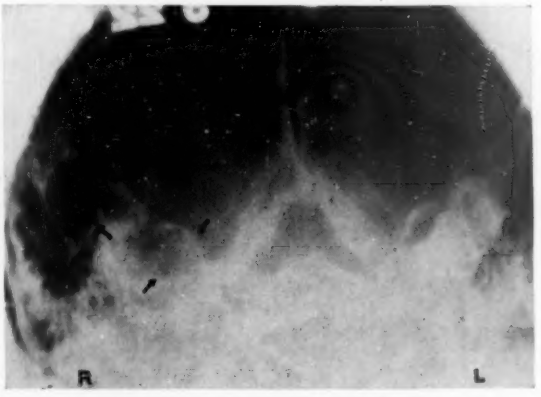


FIG. 4. Case 1. Fronto-occipital projection showing erosion of right petrous pryamid and internal auditory canal, enlargement of the emissary foramen.

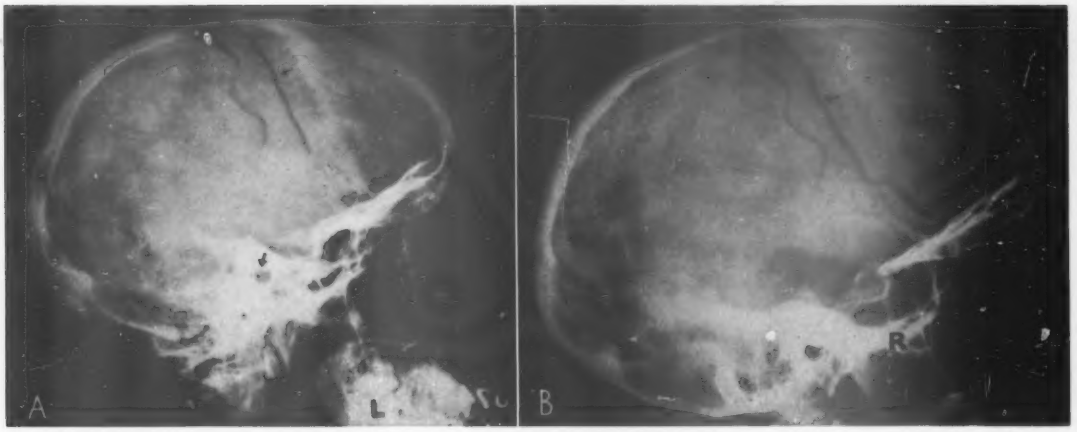


Fig. 5. Case 1. *A*, left lateral view of skull; *B*, right lateral view of skull. Comparison shows increased size of the vascular channels of the left side of the skull, enlargement of the left external auditory meatus, some destruction and sclerosis of the left mastoid cells.

Roentgen examination in the 2 cases herewith presented revealed changes the combination of which is considered diagnostic of angioma of the middle and inner ear. These changes are: (1) increase in size of the vascular channels of the skull on the affected side, (2) enlargement of the groove and foramen of the mastoid emissary vein, (3) erosion of the petrous pyramid, enlargement of the internal and external auditory canals, (4) destruction of the mastoid cells.

Erosion of the petrous pyramid with widening of the internal acoustic meatus is also observed in acoustic neurinoma, occurring in about 80 per cent of cases. The great majority of the latter show in addition slight erosion of the dorsum sellae,[15] a feature not observed in angioma of the tympanic cavity. Enlargement of the external canal is not seen in acoustic neuroma; while in the latter widening of the occipital emissary foramen may occur (15 per cent) as evidence of increased intracranial pressure, no vascular changes are found.[15]

The mastoid emissary foramen normally varies in size measuring from 1 to 10 mm. and it has been stated that widening should not be said to have occurred without a previous roentgen examination for comparison.[15] This, however, is rarely possible. In Case 1, the greatest diameter (measured in the lateral projection which provides the least distortion) was 20 mm.; in Case 11 it was 17 mm. These obviously represent true enlargement.

Increase in size of the vascular channels is most frequently associated with meningioma. It is seen as well in most cases of arteriovenous aneurysm.[15] In neither of these, however, does one find the combination of erosion of the petrous tip, the acoustic canal or the external meatus.

Carcinoma of the middle ear produces symptoms (pain, reduced hearing, repeated

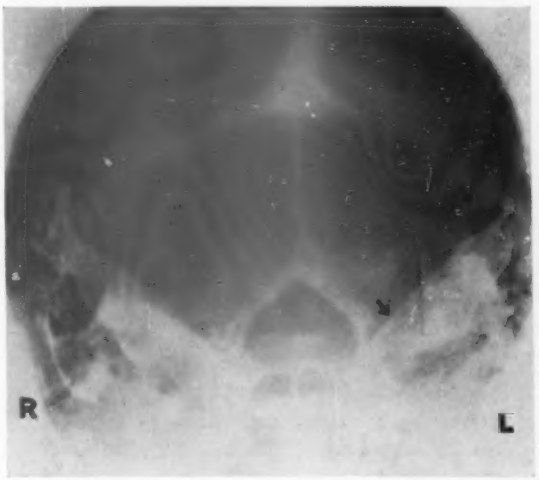


Fig. 6. Case 11. Fronto-occipital projection showing left-sided enlargement of the mastoid emissary foramen, erosion of petrous tip, widening of internal canal.

hemorrhages from the external auditory meatus, frequently facial paralysis) and extensive bone destruction which may closely resemble those produced by angioma. However, the inner compact portion of the petrous pyramid in many cases remains as a knob within the surrounding area of bone destruction.[19]

A smooth enlargement of the external meatus is indicative of long standing pulsating pressure produced by a vascular tumor. Therefore this change should be accompanied by the presence of a visible tumor in the external canal. Changes in the mastoid cells obviously indicate extension of the growth into this area.

Therapeutic measures used in the cases recorded in the literature have not been uniform. One angiosarcoma was treated by instillations of a sclerosing agent[20] with 50 per cent reduction in size in nine months; the final outcome is not known. Radical mastoidectomy (without radium or irradiation) was effective in eradicating polypoid lesions [1,7,13] in one of which the mastoid was found to be involved.[13] In two of the nonpolypoid type and in which there was mastoid involvement death ensued.[2,5]

Surgery plus roentgen therapy was used in one case of hemangiosarcoma[12] with no recurrence at one year. Surgery plus radium therapy was used in a case of endothelial sarcoma; recurrence, however, was present when the patient was seen again seventeen years later.[11] Surgery plus radium and roentgen irradiation is recorded in 3 cases. In one of these, a malignant hemangioma,[3] metastases developed in the glands of the neck and death followed five years after the onset. In 2 cases of hemangio-endothelioma[18] satisfactory results were obtained; 1 patient, with mastoid involvement found at operation is still living and well for seven years. The other patient was free from recurrence when he died of pneumonia two years later.

Of our 2 cases, treated solely by roentgen therapy, one showed temporary symptomatic improvement and frequent recurrences (Case 1) This patient is still engaged at his usual occupation four years after the commencement of treatment. The other patient (Case 11), who had been under observation for only six months, has shown no appreciable improvement.

Furstenberg[12] advocates radical excision of the neoplasm by means of the radical mastoid operation in order to leave the site open for the remainder of the patient's life for inspection and to make possible further treatment with the use of the cautery and irradiation. Schall[18] upholds his contention. The end-results of treatment indicate the correctness of this view, that combined treatment by radical surgery, radium and rotengen therapy offers the best hope of cure.

## SUMMARY

Two cases of angioma of the tympanic cavity are presented. In additon to presenting fairly definite clinical evidence of their presence these tumors can in some cases be recognized by the roentgen findings. These include:

1. Increased size of the vascular channels of the skull on the affected side.
2. Enlargement of the groove and foramen of the mastoid emissary vein.
3. Enlargement of the external auditory canal, erosion of the petrous tip, and enlargement of the internal auditory canal.
4. Destruction of the mastoid cells.

In the polypoid type surgery alone (radical mastoidectomy) is usually effective in eradicating the lesion. In the infiltrative type, particularly those in which mastoid involvement has occurred, surgery should be supplemented by radium and roentgen therapy. Skin damage due to irradiation should be avoided.

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# VENTRICULAR ANEURYSM

## ROENTGENOGRAPHIC AND POST-MORTEM SURVEYS*

*By* JOHN BERNARD SCHWEDEL, M.D., *and* HARRY GROSS, M.D.
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THE finding of a ventricular aneurysm at necropsy is not uncommon. Recognition during life, however, is rare enough to have caused comment in the literature concerning the diagnostic difficulties involved. For instance, Pletnew,[17] in a review of the literature as recently as 1926, found that the diagnosis had been made in life in but 6 out of over 300 reported cases of ventricular aneurysm.

From the post-mortem records of the Montefiore Hospital we collected and analyzed 34 cases of cardiac infarction in which aneurysmal bulges occurred. The aneurysmal sites were carefully noted, and the location of bulges, adhesions, and calcification or other changes recorded. These, together with the roentgen findings, were reviewed in an attempt to correlate the roentgenographic with the necropsy findings. In an extensive but not exhaustive survey, the instances reported in the literature were similarly analyzed. Using the combined findings, we tried, so far as possible, to establish more definite criteria for the diagnosis of ventricular aneurysm.

In the combined material there were altogether 81 cases, though these constituted 89 sites of ventricular aneurysm. In 8 hearts more than one aneurysmal bulge was present. Forty-eight occurred in the anterior or lateral portion of the apex of the left ventricle. In 21 instances the posterior wall of the left ventricle was involved. In 16 of these the bulge was high in the posterior wall. A comparison of our findings with those in the literature showed no striking difference, save for an increased incidence of posterior wall involvement.

Three aneurysms of the right ventricle were found; of these one was on the anterior wall. Five cases of septal bulge were found, of course not visible externally, therefore impossible of roentgen diagnosis. It is seen that most of the bulges occurred either on the low anterior or the low lateral surface of the left ventricle. A smaller but significant group occurred high in the posterior wall of the same chamber.

Roentgenologic diagnosis depends on the contrast of the outline of the heart with that of the air-filled lungs. Surfaces are not visualized unless translated in terms of contour by rotating the patient into various degrees of obliquity. A bulge in the cardiodiaphragmatic region may be more difficult to recognize than that occurring higher in the cardiac outline. A bulge resting on the diaphragm or one occurring in the interventricular septum can therefore never be visualized. A high lateral bulge, in the posteroanterior position, will produce very few difficulties if the left ventricle is adequately identified. Below this point is the inward contraction of the left ventricle during systole; above is the outward pulsation of the conus portion of the right ventricle during the same phase of the cardiac cycle. A bulge low on the lateral contour may be more easily identified by careful inspection during deep inspiration.

Bulges of the posterior wall are somewhat more difficult to identify because of the dense structures in the posterior mediastinum. Careful examination in suspected cases may reveal the bulge extending or breaking the contour of the posterior surface, so that a correct diagnosis may be made.

Repeated examinations will establish the diagnosis and the progress of enlargement of the bulge. The case represented by Figures 1, 2, 3, and 4 began with the angulation which preceded the stage of bulge formation. Repeated examinations showed the progress of the bulge.

A definite incisura or angulation between

* From the Roentgenographic Service of Dr. A. J. Bendick and the Medical Service of Dr. L. Lichtwitz, Montefiore Hospital.

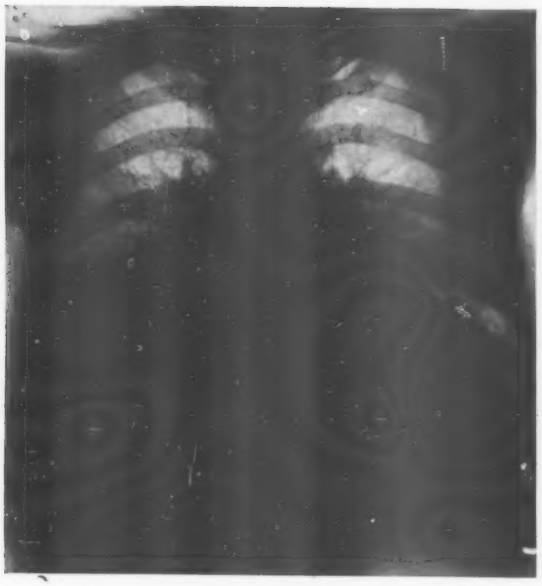

Fig. 1. Angulation precedes bulge seen in subsequent examinations.

Fig. 3. Bulge three years later.

uninvolved portions of the ventricle and the site of ventricular aneurysm was observed three times, once by Assmann[2] and twice by Zadek.[25] These were all just above the diaphragm, and appeared on the left side in the posteroanterior view. Apparently this incisura is similar to that seen in the left oblique view between the right and left ventricles, to the shallow groove between the left ventricle and the left auricle, and also to the point of opposite pulsation identified in the posteroanterior position.

Pericardial adhesions occurred in 19 instances (24 per cent). The existence of pericardial adhesions may be established by the observation of systolic traction or angulation during roentgenoscopy. The angulation of Figure 5 was probably due to a pericardial adhesion, since it is inconceivable that an angulation of this type

Fig. 2. Bulge one and one-half years later.

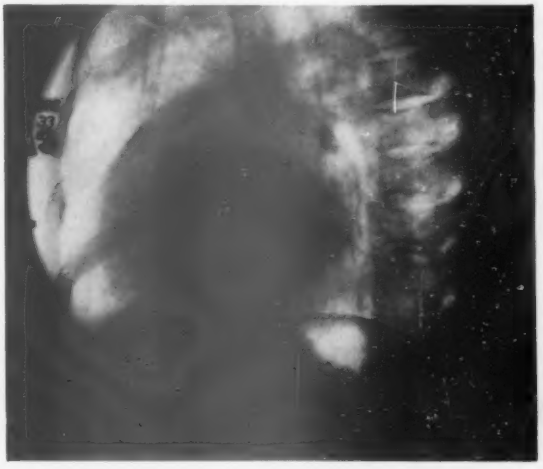

Fig. 4. Increased density as seen in left anterior oblique position

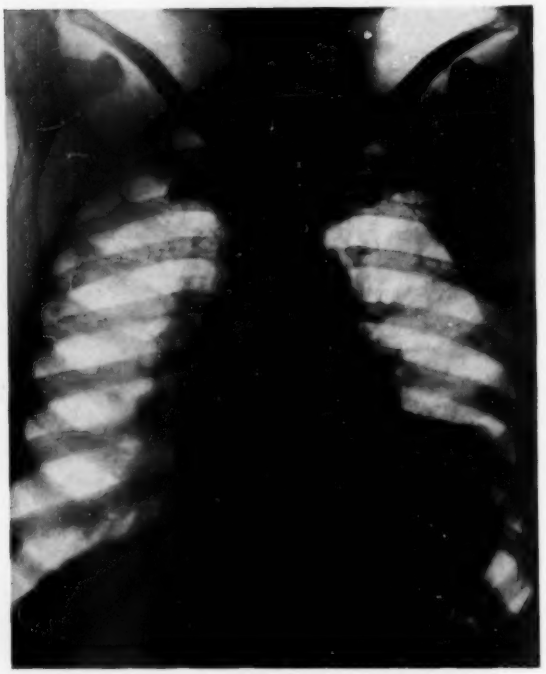

FIG. 5. Striking bulge and angulation formed by ventricular aneurysm.

could be formed by heart muscle under any circumstances.

Increase in density was noted 5 times; of these, 3 were due to calcification. The increase in the density in Figure 4 was very likely due to the superimposition of a lamellated thrombus. In this case it was best demonstrated in the left oblique view.

An important group virtually impossible to diagnose is that in which so massive a portion of the left ventricle is involved that there is enlargement of the entire lateral wall, simulating other types of enlargement of the left ventricle. There were 7 examples of this type of bulge, 2 in the posterior wall and 5 in the lateral wall. In such cases only the presence of additional diagnostic criteria, such as changes in density or pericardial adhesions, could give a clue to the diagnosis. In 2 of the 7 instances, the presence of associated adhesions and increased density actually led to the correct diagnosis during life.

It is noteworthy that the presence of a roentgenoscopic bulge does not always indicate the anatomical site of ventricular aneurysm. In 3 of the reported cases, the 1 of Christian and Frik[5] and 2 of Steel's,[20] the apparent bulge was probably due to enlargement of the left ventricle protruding above an area of cardiac infarction which bulged, but to a less marked degree than the overlying thickened ventricle.

The pulsations reported in the literature and as observed by us were either strong, synchronous, asynchronous, systolic, or contrapulsile. However, the marked variability rendered the type of pulsation unsuitable for use as a diagnostic criterion.

Cardiac infarction with ventricular fibrosis and thinning is quite common. The question arises, however, as to why in the presence of myocardial infarction, which is so frequent, a ventricular bulge is not more common. Several factors preclude the development of a bulge. These are: (1) the size of healed infarcted areas may be too small to bulge; (2) the presence of an endocardial thrombus with or without calcification renders bulging less likely; (3) reinforcement of the outer coats such as thickening of the epicardium and pericardial adhesions also tend to minimize the tendency to bulge formation.

The lesion commonly referred to as ventricular aneurysm is limited to the heart muscle. The word "aneurysm" is a specific term referring to a localized dilatation of an artery. It seems to us that it would be more correct to substitute the term "localized ventricular bulge" for ventricular aneurysm.

## SUMMARY AND CONCLUSIONS

1. Roentgen examination, especially roentgenoscopy, is an adequate method for the detection of ventricular aneurysm.

2. The presence of a bulge or unusual angulation in the cardiac contour should lead to careful examination including rotation into the oblique views to render the bulge contour forming.

3. Since more ventricular aneurysms occur near the diaphragmatic surface, examination is aided by deep inspiration.

4. Accessory diagnostic criteria are (*a*)

Table I

| Cases Reported By | No. of Cases | Massive Involvement Left Ventricle | Lateral | | Anterior | | Posterior | | Pericardial Adhesions | Increased Density | Incisura | Miscellaneous |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | High | Low | High | Low | High | Low | | | | |
| Pletnew[17] | 2 | | | | | 2 | | | | | | |
| Regelsberger[18] | 1 | 1 | | | | | | | 1 | | | |
| Melchart[13] | 1 | 1 | | | | | | | | | | |
| Wiberg[24] | 1 | 1 | | | | | 1 | | 1 | 1 left oblique | | |
| Parade[16] | 1 | 1 | | | | | | | | | | |
| Bauke[4] | 1 | | 1 | | | | | | 1 | 1 | | |
| Kalisch[10] | 1 | | 1 | | | | | | | | | |
| Steel[20] | 4 | | 1 | | | 2* | 1 | | | | | |
| Lutembacher[12] | 2 | | | 2 | | | | | 1 | | | |
| Morris[14] | 5 | | | 1 | | 1 | 1 | | 1 | | | 1 right ventricle<br>1 septum |
| Kraus[11] | 1 | | | 1 | | | | | | | | |
| Christian and Frik[5] | 2 | | | 1* | | 1 | | | | | | |
| Assmann[2] | 1 | | | 1 | | | | | | | 1 | |
| Zadek[25] | 5 | | | 5 | | | | | | | 2 | |
| Strandell[22] | 4 | 1 | | | | 2 | | 1 | | | | |
| Silva[19] | 1 | | | 1 | | | | | | | | |
| Golonsko[8] | 1 | | | | 1 | | | | | | | |
| Jaksch-Wartenhorst[9] | 1 | | | | | 1 | | | | 1 calc. | | |
| Albrecht[1] | 1 | | | | | 1 | | | | | | |
| Eliasoph[7] | 1 | | | | | | | 1 | | | | 1 septum |
| Bacaloglu[3] | 2 | | | | | 1 | 1 | | 1 | | | |
| Cruickshank[6] | 1 | | | | | 1 | | | | | | |
| Sternberg[21] | 7 | | | | 1 | 5 | | | 3 | 1 calc. | | 2 septum |
| Total (literature) | 47 | 5 | 3 | 12 | 2 | 17 | 4 | 2 | 9 | 4 (2 calc.) | 3 | 1 right ventricle<br>4 septum |
| Our cases | 34 | | | 11 | | 8 | 10 entire | 3<br>2 | 10 | 1 calc. | | 2 right ventricle<br>1 septum |
| Grand Total | 81 | 5 | 3 | 23 | 2 | 25 | 14 entire | 5<br>2 | 19 | 5 (3 calc.) | 3 | 5 septum<br>3 right ventricle |

* Low aneurysm with bulge appearing above actual aneurysmal site.

pericardial adhesions; (*b*) increase in density or calcification within the ventricular wall; (*c*) the presence of an angulation or incisura.

5. It is suggested that since the word "aneurysm" refers solely to disease of an artery, the misnomer, "ventricular aneurysm," be replaced by the term, "localized ventricular bulge."

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# THE RESPIRATORY MOTION OF THE LUNG DURING ARTIFICIAL PNEUMOPERITONEUM TREATMENT*

## A ROENTGENOLOGICAL STUDY

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THERE is no report in the medical literature dealing with the systematic investigation of the effect of pneumoperitoneum upon the respiratory motion of the lung in human beings. For this reason, I have investigated this subject in 40 individuals treated by this method for their pulmonary tuberculosis. A comparable study[1] was carried out by me previously in which data were presented concerning the immobilizing effect of artificial pneumothorax. It was found by roentgenological measurements that a limitation of the respiratory motion of the relaxed lung was absent in a surprisingly large percentage of the cases. Furthermore, it was ascertained that the motion of the diseased portion of the treated lung was closely similar to the motion of the entire lung before treatment in 18.2 per cent, and it was greater than the motion of the entire lung before treatment in 27.3 per cent. In other words, the artificial pneumothorax had no immobilizing effect upon the diseased portion of the lung in 45.5 per cent. I[2] have also studied the question of pulmonary rest after surgical paralysis of the phrenic nerve, and found that the motion of the lung was reduced in 60 per cent, it remained unchanged in 16.7 per cent, and increased in 23.3 per cent of the cases. In other words, the anticipated pulmonary rest following phrenic nerve block was not accomplished in 40 per cent of the cases.

In the present study, the extent of the respiratory motion of the lung was estimated according to a roentgenological method devised by Hurtado and Fray[3] for the determination of the respiratory expansion of the chest. They found that the degree of chest expansion can be calculated from the relationship between the roentgenological lung fields at maximum expiration and inspiration. The roentgenograms used in this work were taken at the end of the two respiratory phases, in the upright position, on two films, from a distance of 6 feet. The area of the lung fields was measured by means of a planimeter, the tracer arm of which was moved along the following course: along the inner aspect of the ribs from the left axilla to the left half of the diaphragm, the right half of the diaphragm, the right lateral border of the lung, right apex, and across the spine to the starting point at the left apex. A line was drawn corresponding to the middle of the trachea and the mediastinum. Thus it was possible to measure the areas of the right and left lung separately.

The figures on the differential wheel of the planimeter indicate areas in square centimeters. The roentgenological respiratory ratio was calculated according to the following formula: (Roentgenological area at maximum expiration/Roentgenological area at maximum inspiration)$\times$100. This ratio is inversely proportionate with the extent of the respiratory excursions; the higher the ratio, the smaller the motion, and vice versa.

Forty patients who were treated by pneumoperitoneum for pulmonary tuberculosis were analyzed. Of these, 11 were in the moderately advanced stage and 29 in the far-advanced stage according to the classification of the National Tuberculosis Association. Measurements taken before and after treatment were compared. Measurements were made in 31 cases after the first treatment, in 1 after the second, in 7 after the third, in 6 after the fourth, in 2 after the fifth, in 8 after the sixth, in 2 after the seventh, in 2 after the eighth, in 8 after

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the tenth, in 1 after the eleventh, in 3 after the twelfth, in 1 after the fourteenth, in 2 after the fifteenth, in 4 after the sixteenth, in 1 after the twentieth, in 4 after the twenty-second, and in 1 after the twenty-third treatment. Thus, including the films taken before treatment, 248 chest roentgenograms were measured. The amount of injected air at each treatment varied from 500 to 1,000 cc. The treatments were given by the subumbilical route: the site of injection was three fingers' breadth below and to the left of the umbilicus. The treatments were repeated at weekly intervals at the beginning, and two weeks apart when the pneumoperitoneum was well established.

Hurtado and Fray[3] state that if the roentgenological respiratory ratio is higher than 72, a definite reduction in chest expansion may be suspected. I have found that the ratio of the more diseased lung before treatment varied from 71 to 100. There were none between 60 and 69, 4 between 70 and 79, 15 between 80 and 89, and 14 between 90 and 100. The ratio of the less diseased lung was found to be between 60 and 69 in 2, between 70 and 79 in 8, between 80 and 89 in 14, between 90 and 100 in 9. Cases with about equal distribution of the disease on both sides were found in the following groups: right lung, between 70 and 79, 2; between 80 and 89, 3; between 90 and 100, 2; left lung, between 70 and 79, 1; between 80 and 89, 5; between 90 and 100, 1.

It was noted that the motion of the lung was reduced by from 8 to 18 points in instances with considerable motion before treatment, that is, in the group of roentgenological respiratory ratio 60–69. In 34 observations in the roentgenological respiratory ratio group 70–79, the motion remained the same as before treatment in 22 (64.7 per cent), increased in 5 (14.7 per cent), and decreased in 7 (20.5 per cent). The decrease, calculated in roentgenological respiratory ratios, varied fro . , 11 points, with an average of 8.4. In the roentgenological respiratory ratio group 80–89, the analyzed cases comprised 83 instances; of these the motion was the same as before treatment in 46 (55.4 per cent), increased in 15 (18 per cent), and decreased in 22 (26.5 per cent). The decrease varied from 6 to 18 points, with an average of 9.5. There were 47 observations made in cases with very slight respiratory excursions prior to treatment, the roentgengenological respiratory ratio group 90–100. Of these the motion of the lung remained the same as before treatment in 22 (46.8 per cent), increased in 15 (31.9 per cent), and decreased in 10 (21.2 per cent). The decrease varied from 6 to 9 points with an average of 6.9. All four roentgenological respiratory ratio groups together include 168 measurements. Of these the respiratory motion remained uninfluenced by pneumoperitoneum in 90 (53.5 per cent), increased in 35 (20.8 per cent), and decreased in 43 (25.6 per cent). The interpretation of these figures must be made with two potential factors in mind: first, the possible variations in respiratory effort, although utmost care was exercised in taking the films at the end of maximum inspiration and expiration; and secondly, the probable presence of some involuntary compensatory effort because of the elevated position of the diaphragm and because of the pulmonary relaxation and diminished lung volume caused by the pneumoperitoneum.

One would expect that with the increasing number of treatments the respiratory motion of the lung is gradually decreased. At first glance, data presented in Table 1 might give a different impression. For instance, after 15 treatments there were 4 cases with increased motion and none with decreased motion. However, the fact that these 4 instances represent 2 individuals in whom *both* sides showed increased motion indicates that this increase was most likely induced by an increased respiratory effort. In one of these patients the respiratory motion was unchanged after the first and third treatments. In the other case, four months elapsed between the first and fifteenth treatment; it is reasonable to as-

sume that the improved general and pulmonary condition of the patient might have contributed to the better respiratory capacity. An increased respiratory effort was the cause of the increased motion of both lungs in a patient studied after the second treatment, and in a patient after the twentieth treatment.

The influence of pulmonary involvement upon the motion of the lung during pneumoperitoneum treatment was also studied. In 68 instances the extent of the disease in one lung was considerably greater than in the opposite lung. It was found that the motion on the less involved side remained unchanged in 38 (55.8 per cent), increased in 14 (20.6 per cent), and decreased in 16 (23.5 per cent). On the more diseased side, the motion remained the same as before treatment in 37 (54.4 per cent), increased in 14 (20.5 per cent), and decreased in 17 (25 per cent). There were 16 instances in which the tuberculous process was of about equal extent in the right and left lungs. On the right side, the motion remained the same in 7, increased in 3, and decreased in 6. On the left side there was no change in the motion in 8, the motion increased in 4, and decreased in 4. There were 7 instances with 14 measurements in which both the diseased and the "good" lung showed increased respiratory motion that undoubtedly indicates increased respiratory effort on the part of the patient. In patients with equal disease in both lungs, the motion was increased on both sides in 1 case, and on one side in 5. Pleural thickening or contraction of the chest was present on the side where the motion did not increase while increase was noted on the opposite side. It was rather surprising to find 7 cases in whom the more involved

Table I

| Roentgenological Respiratory Ratio | Number of Treatments | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | | 2 | | | 3 | | | 4 | | | 5 | | | 6 | | | 7 | | | 8 | | | 10 | | | 11 | | | 12 | | |
| | I | D | S | I | D | S | I | D | S | I | D | S | I | D | S | I | D | S | I | D | S | I | D | S | I | D | S | I | D | S | I | D | S |
| 60–69 | | 2 | | | | | | | | | | | | | | | | | | 1 | | | | | | 1 | | | | | | | |
| 70–79 | | 3 | 9 | | | | | | 4 | 1 | 1 | | | | 1 | | 1 | 2 | | | | | | | 1 | | 3 | | 1 | | | |
| 80–89 | 3 | 9 | 18 | | | | | 3 | 4 | 1 | 1 | 4 | 1 | | | 2 | 2 | 3 | | | | 1 | | 1 | | 2 | 6 | | 1 | 2 | 2 | 2 | 2 |
| 90–100 | 4 | 2 | 12 | 2 | | | | 2 | 1 | 2 | 2 | | 1 | | 1 | 3 | 1 | 2 | 1 | 1 | 1 | 2 | | | | 1 | 2 | | | | | | |
| Total of Changes | 7 | 16 | 39 | 2 | | | | 5 | 9 | 4 | 4 | 4 | 2 | | 2 | 5 | 4 | 7 | 1 | 2 | 1 | 3 | | 1 | 1 | 4 | 11 | | 1 | 2 | 2 | 2 | 2 |
| Percentage of Changes | 11.2 | 25.8 | 62.9 | 100 | | | | 35.7 | 64.2 | 33.3 | 33.3 | 33.3 | 50 | | 50 | 25 | 31.2 | 43.7 | 50 | 25 | 25 | 75 | | 25 | 6.2 | 25 | 68.7 | | 33.3 | 33.3 | 33.3 | 50 | 50 |
| Total of Observations | 62 | | | 2 | | | 14 | | | 12 | | | 4 | | | 16 | | | 4 | | | 4 | | | 16 | | | 2 | | | 6 | | |

| Roentgenological Respiratory Ratio | Number of Treatments | | | | | | | | | | | | | | | | | | Total of Changes | | | Total of Observations |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 14 | | | 15 | | | 16 | | | 20 | | | 22 | | | 23 | | | | | | |
| | I | D | S | I | D | S | I | D | S | I | D | S | I | D | S | I | D | S | I | D | S | |
| 60–69 | | | | | | | | | | | | | | | | | | | | 4 | | 4 |
| 70–79 | | | | 2 | | | 1 | 1 | | | | | 1 | | 2 | | | | 5 | 7 | 22 | 34 |
| 80–89 | | | | 2 | | | 2 | 3 | | 2 | | | | | 4 | 1 | 1 | | 15 | 22 | 46 | 83 |
| 90–100 | | | 2 | | | | | 1 | | | | | | 1 | | | | | 15 | 10 | 22 | 47 |
| Total of Changes | | | 2 | 4 | | | 3 | 5 | | 2 | | | 1 | 1 | 6 | 1 | 1 | | 35 | 43 | 90 | 168 |
| Percentage of Changes | | | 100 | 100 | | | 57.5 | 62.4 | | 100 | | | 12.5 | 12.5 | 75 | 50 | 50 | | 20.8 | 25.5 | 53.5 | |
| Total of Observations | 2 | | | 4 | | | 8 | | | 2 | | | 8 | | | 2 | | | | | | 168 |

Index to abbreviations: I = respiratory motion increased; D = respiratory motion decreased; S = respiratory motion the same as before treatment. The corresponding figures indicate the number of observations.

side showed an increased motion while the less involved side showed no change, or a diminution in motion. A survey of these cases revealed considerable disease in the "good" lung, although its extent was less than on the opposite side. The underlying cause of this discrepancy is not known to us. The extent of emphysema and pleural adhesions was practically the same on both sides in these cases.

The effect of the motion of the diaphragm upon the motion of the lung during pneumoperitoneum treatment was also analyzed. There were 72 instances in which the motion of the diaphragm was greater during treatment than before treatment. In this group, the motion of the lung remained the same in 40 (55.5 per cent), increased in 25 (34.7 per cent), and decreased in 7 (9.7 per cent). The diaphragmatic motion remained unchanged during treatment in 21 instances. Of these the motion of the lung remained the same in 11 (52.3 per cent), increased in 5 (23.8 per cent), and decreased in 5 (23.8 per cent). In 75 instances, the diaphragmatic motion was decreased during treatment. In this group, the motion of the lung remained unchanged in 41 (54.6 per cent), increased in 3 (4 per cent), and decreased in 31 (41.3 per cent). These data show that the limitation of the motion of the diaphragm is an important factor in reducing pulmonary motion during pneumoperitoneum treatment. It is also evident that in some instances, a well-established pneumoperitoneum causes a dissociation between the respiratory functions of the diaphragm and the upper ribs. This is well illustrated by the fact that increased motion of the diaphragm was accompanied by diminished respiratory excursions of the lung in 9.7 per cent, and that decreased motion of the diaphragm was associated with increased respiratory motion of the lung in 4 per cent.

## DISCUSSION

The conception that in the treatment of pulmonary tuberculosis the beneficial effect of mechanical measures, such as artificial pneumothorax, the surgical paralysis of the phrenic nerve, and artificial pneumoperitoneum is attributable mainly to their immobilizing effect must be revised. Besides a substantial number of cases in which reduction of the respiratory motion is noted following these interventions there is another large group of instances in which favorable clinical response is observed without immobilization, or even in the presence of increased respiratory motions. These facts suggest that although functional rest is desirable it is not an indispensable factor in establishing a cure. Observations that I have made on patients in whom accurate measurements of the pulmonary motion were carried out before and after the above-mentioned mechanical measures have led me to the conclusion that, in all these instances, the relaxation of the lung tissue is of greater significance than any other effect of these treatments.

The relaxation of the lung is followed by an increased drainage of inflammatory products from cavities and from the bronchial tract. This is likely to lead to a diminution of toxic symptoms, and decrease in cough. Pulmonary relaxation, accompanied by increased freedom from cough, means a better chance for the defense and repair of the diseased tissues. Decrease in the size of cavities or their complete obliteration is greatly aided by pulmonary relaxation. An effective relaxation of the diseased lung is followed by a passive hyperemia and increased carbon dioxide content of the tissues. Empirical and experimental observations quoted before[4] established these two factors as antagonistic to the development of tuberculosis and as favorable for the healing of tuberculosis.

I have shown in a previous work[5] that artificial pneumoperitoneum given at regular intervals is capable of inducing a degree of relaxation of the lung that is known to be sufficient for improving the resistance, defense, and repair of the pulmonary tissues, and thus it brings about a condition which is favorable to the healing process of tuberculous lesions.

## CONCLUSIONS

1. Roentgenological measurements and analysis of 248 chest films are presented that were taken for the purpose of determining the respiratory motion of the lung during pneumoperitoneum treatment of pulmonary tuberculosis.

2. Although certain unavoidable technical limitations, such as variations in volitional respiratory effort during serial observations, and changes in the pulmonary disease (improvement or progression) detract to some extent from the value of these findings, their interpretation throws some light upon the mechanics of artificial pneumoperitoneum.

3. The respiratory motions were reduced considerably in patients whose lungs showed marked respiratory excursions before treatment. In cases where the respiratory motions before treatment were moderate, restricted, or slight, the extent of the motion was reduced by pneumoperitoneum in 20.5, 26.5, and 21.2 per cent, respectively. The remaining instances showed either no change or increased motion. Out of 168 measurements comprising the four groups with different roentgenological respiratory ratios the pulmonary motion was decreased in 25.6 per cent, remained unchanged in 53.5 per cent, and increased in 20.8 per cent. The latter might be accounted for by increased respiratory effort.

4. An increased respiratory effort is suggested by the fact that the respiratory excursions of the diaphragm were greater during treatment than before treatment in 72 out of 168 instances. Out of 75 instances in which the diaphragmatic excursions were restricted during treatment, the respiratory motions of the lung were increased in 4 per cent, remained the same in 54.6 per cent, and decreased in 41.3 per cent.

5. Because of the influence of the diaphragm upon the respiratory motion of the lung, it must be emphasized, as I have pointed out before,[6,7] that in unilateral cases better results follow pneumoperitoneum if it is preceded by a phrenic nerve block. As a matter of fact, the most startling results I have seen in my experience with this method were in patients in whom artificial pneumoperitoneum was used after surgical paralysis of the phrenic nerve.

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# PANCREATIC LITHIASIS

## WITH REPORT OF A CASE

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ALTHOUGH pancreatic lithiasis is not common, the condition should be of unusual interest to the roentgenologist because the roentgen ray offers the best method of preoperative diagnosis. An estimated 200 cases have been reported but remarkably few of these have been correctly diagnosed except at operation or by post-mortem examination. The stones are usually of high calcium content, being composed mainly of calcium carbonate. This fact led Mayo Robson, in 1904, to suggest the use of the roentgen ray in their diagnosis. It was not until 1912, however, that Assmann, after finding pancreatic calculi at post mortem, was able to demonstrate them on roentgenograms made of the patient before death. That the condition is probably more common than reported cases would indicate is evidenced by the fact that Morrison and Bogan, in the reexamination of the films of 6,000 consecutive cases, found 4 patients with shadows in the pancreatic region which they felt were due to pancreatic stones. In addition to the case reported here, I have also made the roentgenographic diagnosis of pancreatic lithiasis in 2 patients seen during the last two months.

The clinical aspects of reported cases of pancreatic lithiasis have been admirably reviewed by Seeger, Sennett, Bost, Faust, and others, but they are in no way characteristic of the condition. Pain appears to be the most common symptom but it is variable in character and location. Steatorrhea, glycosuria and jaundice may or may not be associated symptoms. Tuberculosis has been present in several reported cases but whether this is related or coincidental has not been established. The chemical analysis of pancreatic stones found in the stool has led to the correct diagnosis in a few instances. The lack of familiarity with the location and roentgen appearance of pancreatic stones, as occurred in our first case, has no doubt been responsible for many failures in diagnosis. Obviously pancreatic lithiasis does not occur often enough to allow any one person to study the condition adequately from his own cases. I have attempted, therefore, to determine the appearance of pancreatic lithiasis by studying reproductions of roentgenograms accompanying reported cases. In addition to my own proved case I have been able to find 29 cases in which the reproductions were of sufficient clarity to give a fair idea of the roentgenographic appearance. This group does not include all reported cases showing roentgenograms but only those available to me in the University Library.

From this series of 30 cases it is observed that location is a very important factor in arriving at a diagnosis. In the great majority of cases the stones lay below a horizontal plane passing through the upper margin of the body of the first lumbar vertebra and above a horizontal plane passing through the lower margin of the body of the third lumbar vertebra. In 21 cases of this series the stones were between these two planes. In only 9 instances were stones seen above the upper plane, and in no instance were stones observed below the lower plane.

As is well known, the duodenum forms a loop around the head of the pancreas and when pancreatic calculi are suspected, it is well to visualize the duodenum to observe its relationship to the suspected shadows. Barium is not a satisfactory medium because the barium in the stomach is likely to obscure any stones which may be present. Carnot and Engelstad and Römcke independently have suggested that a duodenal tube be passed before

taking roentgenograms to give the relationship of the duodenum to the pancreatic head. In their cases this has been very satisfactory and has not obscured the pancreatic calculi. It is also advisable, if possible, to visualize the gallbladder and make pyelographic studies to establish the anatomic relationship of these organs to any suspected shadows. In size, pancreatic stones vary from very minute calculi comparable to grains of sand to large calculi measuring as much as 4 or 5 cm. in diameter. From the operative and post-mortem examinations it has been found that these stones usually lie within the main pancreatic duct and its smaller radicles. Pancreatic stones are all very dense, and may even be observed on the roentgenographic film when overlying the vertebral bodies. They are usually more dense than the calcium-containing gallstones although they do not appear to differ appreciably in density from renal calculi. It may be difficult or impossible in certain instances to differentiate them from calcified lymph nodes.

From the roentgenographic standpoint pancreatic lithiasis can conveniently be divided into four groups:

(*1*) *Multiple Calculi:* These are most common and were present in 24 of the 30 cases. In size, these calculi vary from minute concretions comparable to grains of sand to larger masses 1 to 2 cm. in diameter. They are very irregular in shape, are not facetted, and usually occupy the main duct together with the lesser radicles. The contour of the entire pancreas may, in fact, be outlined, the stones in the head being lower and located on the right side lateral to the spine and those in the neck, body and tail extending upward and to the left across the midline. When the pancreas is outlined in this manner the roentgen appearance is quite characteristic. Although usually fewer in number, as many as several hundred stones may be present in cases falling into this group.

(*2*) *Single Calculi:* A single calculus was present in 3 cases. In 2 of them the stone was located in the region of the head and in one it was located in the body. In this type position is the most important factor in diagnosis. Graham Hodgson was able to diagnose such a single stone the size of a large oat from the roentgen film because the position of the shadow suggested that it must be within the duct of Wirsung. His diagnosis was confirmed by operation.

(*3*) *Multiple Facetted Calculi:* Stones of this type were present only in the case reported by Friedrich and in my own case. They closely resemble gallstones in size and shape and even have less dense centers. In my case the presence of these stones lying just to the right of the spine in the position and direction corresponding to the course of the pancreatic duct together with a visualized gallbladder should have led to an unqualified diagnosis.

(*4*) *Large Fragmented Calculi:* In one case, that of Wolf and Tietze, there appeared to be a large fragmented stone which formed a cast of the dilated pancreatic duct in the region of the head and neck of the pancreas. Here again position should be an important factor in diagnosis.

### CASE REPORT

S. L., a girl, aged fifteen, entered the hospital on October 6, 1936, complaining of pain in the "right side," hip, and leg.

*Present Illness.* The patient stated that she has had attacks of severe "sticking" pain in the right lower quadrant, accompanied by nausea and vomiting, since she was three years old. These attacks have occurred at irregular intervals, from two to four months apart, and last usually about one week. The attacks have grown progressively worse and more frequent. She had an appendectomy one year ago with no relief. The last attack was six weeks ago. Since that time there has been a dull, aching pain almost continuous in the right lower quadrant, with slight soreness. For the past three weeks she has noticed intermittent aching in the right thigh with some discomfort about the hip. There was no pain in the knee and there was only slight difficulty in walking.

*Past History.* This was essentially negative except for the present illness. There was no history of jaundice.

FIG. 1. This roentgenogram demonstrates the relationship of the pancreatic calculi to the visualized gallbladder and lumbar spine. Facetted calculi of this type are exceedingly uncommon in cases of pancreatic lithiasis.

*Family History.* The father died at the age of thirty-four from a stroke. He was said to have had "sugar diabetes." Mother is living but is in poor health due to a bladder tumor.

*Physical Examination.* The patient was a young white girl appearing somewhat older than the stated age of fifteen. She was in no acute distress. The physical examination was essentially negative except for moderate tenderness over the right lower quadrant and about the costovertebral angle posteriorly. Pelvic examination showed a third degree retrodisplacement of the uterus. There were no masses, tenderness or discharge. The right leg was held partly flexed at the knee and was somewhat painful to rotation and extension.

*Laboratory Examinations.* Blood examination showed 7,500 white blood cells; hemoglobin 90 per cent; red blood cells 4,300,000. Blood chemistry—urea nitrogen, 10.5; creatinine, 1.0. Urine—no albumin or sugar; microscopic examination showed an occasional white blood cell.

*Roentgen Examination.* Flat preliminary film of the urinary tract showed seven facetted calculi with less opaque centers. The upper calculus was overlying the right inferior margin of the body of the first lumbar vertebra and the remaining stones extended in a curved line outward and downward lateral to the body of the second lumbar vertebra. The last stone lay 1.5 cm. lateral to the right margin of this vertebra. The largest stone measured 1 cm. in diameter and the smallest 0.5 cm. in diameter.

Retrograde pyelograms showed the kidney pelves and calyces on both sides to be normal.

Cholecystography (Fig. 1) showed the gallbladder to be well visualized and lying in its normal position under the lower edge of the liver and lateral to the calculi.

In spite of these findings it was felt that the supposedly typical appearance of the stones marked them as biliary calculi located either within an anomalous biliary system or dilated common duct.

An exploratory operation was performed on October 20, 1936. Stones were palpated in the pancreas and were removed. A T-tube was left within the duct.

A section of tissue was removed from the pancreas which on microscopic examination showed scarring. The calculi were analyzed and found to be composed of an outer heavy shell of calcium carbonate surrounding a small core of

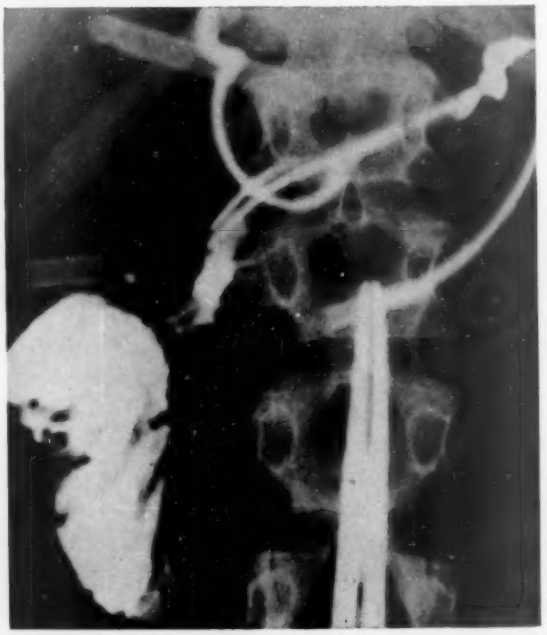

FIG. 2. This film shows the pancreatic duct and duodenum outlined by lipiodol injected through the T-tube. By comparing with Figure 1 it is obvious that the stones were located in the portion of the duct passing through the head of the pancreas.

soft material, the nature of which was unknown. A roentgen examination following the injection of lipiodol in the T-tube (Fig. 2) demonstrated the pancreatic duct to be well outlined and it was observed that the stones obviously occupied the portion of the duct within the head of the pancreas. The patient was discharged on November 7, 1936. Convalescence was uneventful and she had no difficulty until May 3, 1937, at which time she had an attack of pain with vomiting similar in character to her previous attacks. The patient had seven succeeding attacks and was readmitted on July 27, 1937. Roentgen examination at this time was negative. She was re-explored, the pancreatic duct opened and a stricture found near the duodenum. This was dilated and another T-tube inserted. Convalescence again was uneventful. She was discharged on August 30, 1937, with the T-tube in the pancreatic duct. This was removed when the patient was readmitted on December 11, 1937. While there has been some backache there has been no recurrence of attacks of pain since the dilatation of the stricture.

## DISCUSSION

This case appears to be of unusual interest because to my knowledge this is the youngest patient on record having pancreatic lithiasis.

The presence of facetted pancreatic calculi with less dense centers is also exceedingly uncommon even among cases of pancreatic lithiasis. However, in retrospect the diagnosis should have been made because of the location of the stones which corresponded to the course of the duct of Wirsung through the head of the pancreas.

## SUMMARY

1. The clinical findings in pancreatic lithiasis are in no way characteristic.

2. The roentgen ray offers the best method of preoperative diagnosis.

3. Location is a very important factor in making a diagnosis. In the majority of cases pancreatic stones lie below a horizontal plane passing through the upper margin of the first lumbar vertebra and above a horizontal plane passing through the lower margin of the third lumbar vertebra.

4. In establishing the relationship of suspected shadows the gallbladder, duodenum, and kidneys should be visualized.

5. Pancreatic lithiasis occurs in four groups:

(1) Multiple irregular calculi.
(2) Single calculi.
(3) Multiple facetted calculi.
(4) Large fragmented stones forming a cast of the pancreatic duct.

6. A case is reported occurring in a girl, aged fifteen.

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# SKELETAL METASTASIS IN TERATOMA OF THE TESTICLE

## REPORT OF TWO CASES

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METASTASIS to bone in teratoma of the testicle is rare. Geschickter and Copeland report only one instance of metastasis to the bone in 42 cases. In a series of 100 cases reviewed, only 2 metastatic lesions were found.

### REPORT OF CASES

CASE 1 (No. 62961). J. R. W., a white male, aged forty, occupation farmer, was admitted July 30, 1935, for treatment of metastasis from teratoma of testicle formerly diagnosed.

*Family History*. Essentially negative.

*Past History*. Negative.

*Genitourinary Report July 31, 1935*. This patient was operated upon March 26, 1935, and the right scrotal content removed for tumor following a course of deep external irradiation. Patient states that, following his operation, he gained weight and felt well until the last of May, 1935, when he began to develop pain in the right hip and right pelvis, which radiated down the right leg. He has lost 40 pounds since May. There have been no chest pains, cough, nor pain in the back.

On examination, the kidney regions are negative. The bladder region is negative, but there is a mass in the right abdomen opposite the right anterior superior spine, which is firmly fixed, somewhat tender, and does not move with respiration. The genitalia are negative except for absence of the right scrotal content. There is no adenopathy. The urine is clear in both portions, and essentially negative for cellular elements. The prostate and vesicles are normal to palpation, and expressed fluid is negative.

*Laboratory Findings*. Urinalysis: July 30, 1935—Reaction, acid; specific gravity, 1.016; color, straw; albumin and sugar, negative; white blood cells, red blood cells, casts and epithelial cells, none found. Wassermann and Kahn tests were negative. Red blood cells, 4,860,000; white blood cells, 9,600; hemoglobin, 85 per cent. Special examinations of urine July 31, 1935—prolan A, 200 M.U./L.

*Roentgen Findings*. Roentgenogram of the chest on August 8, 1935, disclosed the bony framework, heart, diaphragm and trachea to be normal in appearance. The right lung presents an annular shadow of increased density, measuring 2 cm., in the second anterior inter-

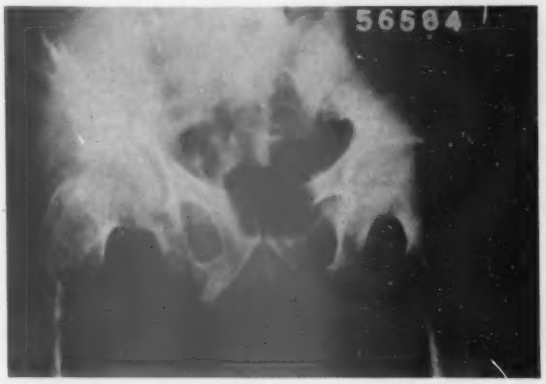


FIG. 1. Irregular rarefaction of the neck of the femur, with evidence of a pathological fracture extending through the lesser trochanter. An abnormal density is seen extending over the left hip and ilium suggesting a pathological process in this area. The right sacroiliac joint presents a circumscribed annular shadow of increased density measuring 1 cm.

space. An ill-defined, annular shadow is noted at the left cardiophrenic angle. Comparison with film taken February 21, 1935, reveals the lesion at the right base, present at that time, to have disappeared and to have been replaced by the one mentioned above. A roentgenogram of the pelvis shows evidence of irregular rarefaction at the neck of the right femur. There is evidence of a pathological fracture extending through the lesser trochanter suggestive of metastatic new growth. There is an abnormal density extending over the left hip and ilium suggesting a pathological process in this area. The right sacroiliac area presents a well circumscribed annular shadow of increased density measuring 1 cm. in its greatest diameter. Due to the patient's inability to cooperate, the films of the skull are not entirely satisfactory. An annular shadow, of decreased density, is

seen in the left parietal region, measuring about 4 cm. in diameter, suggesting a metastatic new growth.

FIG. 2. A generalized demineralization of the bones of the left ilium and ischium and upper third shaft of the left femur is seen. There is a pathological fracture crossing the shaft of the femur.

*Diagnosis.* (1) Teratoma of the testis, postoperative, with metastasis to chest, abdomen and pelvis; (2) absence, acquired, right scrotal content; (3) postoperative orchidectomy for malignant tumor, with metastasis to the abdomen; (4) otitis media, chronic, catarrhal, bilateral; (5) astigmatism, hyperopic, bilateral, moderate.

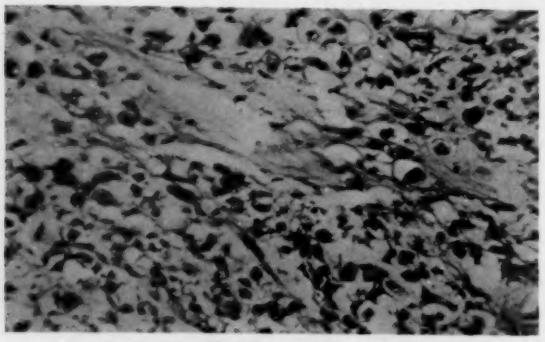

FIG. 3. Photomicrograph showing large round and polyhedral cells of embryonal type with vesicular hyperchromatic nuclei. The stroma except near the center is scanty, and strands of lymphoid tissue were prominent under low power.

He remained in hospital for treatment of teratoma testis, postoperative, with metastasis to chest, abdomen and pelvis. On September 3, 1935, he developed a pathological fracture of right femur, due to metastasis. His condition was critical and the prognosis was hopeless. Patient died on October 17, 1935.

CASE II (No. 56960). T. W. C., a white male, occupation printer, was admitted on October 3, 1934, for hospital treatment of arthritis.

*Chief Complaint.* "Knot" in the back of left hip.

*Family History.* Father died at age of sixty-four of heart trouble. Mother living and well at sixty-three. No history of tuberculosis, cancer or insanity.

*Past History.* Measles, mumps, diphtheria, whooping cough, chickenpox, when a child. Herniotomy at eleven years of age. Denies venereal disease.

*Present Illness.* About six months before admission a painful knot developed in posterior

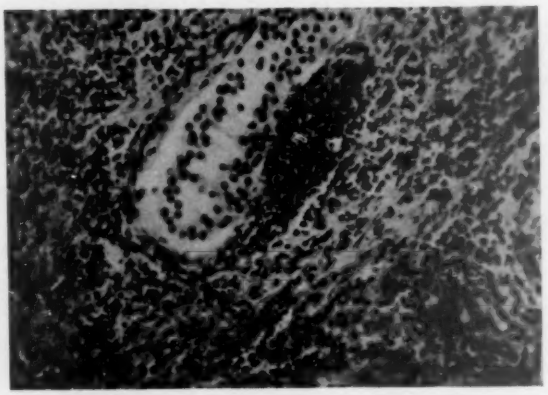

FIG. 4. Photomicrograph showing strands of lymphoid tissue. Low power.

aspect of left hip. Teeth were roentgenographed; three were found abscessed and impacted, and were extracted. A diagnosis of arthritis was made, which gradually grew worse until it involved the knees and right shoulder. Five weeks before admission the right knee "cracked" since which time weight bearing has been impossible, and the left leg became smaller than the right.

*Physical Examination.* On October 4, 1934, an emaciated male reported for examination on a stretcher. The various systems including the lymph glands and genitalia were essentially negative. Because of weakness, standing or sitting was impossible. There was normal range of motion in the various joints of the upper extremities, with discomfort on manipulation

of the right shoulder. There was a hard, nodular, firmly attached mass over the right scapula near the posterior axillary line about 10 cm. in diameter. There was a definite palpable irregularity in the contour of the left femur at the junction of the upper and middle third with shortening and palpable thickening and infiltration of the left side of the ilium. There was much tenderness at these points, and no effort was made to manipulate the lower extremity.

*Laboratory Findings.* Urinalysis, reported monthly from October, 1934, to June, 1935, was essentially negative except for a gradual but continuous increase in the white blood cells. Bence-Jones bodies, negative. Blood counts, done monthly from October, 1934, to June, 1935, showed a gradual decrease in red blood cells from 4,200,000 to 1,500,000, with a corresponding decrease in hemoglobin from 80 per cent to 35 per cent. The average differential count was: polymorphonuclear leukocytes, 68 per cent; lymphocytes, 27 per cent; large monocytes, 5 per cent. Blood chemistry: calcium—15.4 mg. per 100 cc. taken on March 18, 1935; phosphorus—2.4 mg. per 100 cc., same date. Wassermann and Kahn tests, negative.

*Roentgen Findings.* Roentgenographic examination of lumbar spine and pelvis on December 22, 1934, shows a general demineralization of the bones of the left ischium, ilium and upper third shaft of the femur. A pathological fracture is seen crossing the shaft of the femur, 3 cm. below the lesser trochanter. Summary: Probable metastatic malignancy.

The bedside roentgenological examination of the left femur on January 16, 1935, shows evidence of a pathological fracture 2 inches below the lesser trochanter, alignment poor, characterized by outward bowing and overriding. There are bony changes involving the ischium.

Bedside roentgenographic examination on January 21, 1935, reveals destruction of the left ilium, ischium and upper third of the shaft of the femur, suggestive of malignant disease. There is no roentgen evidence of involvement of the lumbar spine.

The roentgen examination of the chest on March 18, 1935, shows the bony framework, diaphragm and costophrenic sinuses to be within the normal limits. The cardiac image shows no alteration from the normal in size, shape or position to suggest organic pathology. The lung fields are radiant throughout all lobes. There is no demonstrable roentgen evidence of metastasis. Summary: Lungs normal. Heart normal.

Roentgenographic examination of left mandible on April 11, 1935, shows several small areas of decreased density, about 5 cm. anterior to the angle of the mandible. These areas represent loss of bone tissue, but do not extend throughout the entire thickness of bone. Probable metastasis, left mandible, with evidence of bone destruction.

*Diagnosis*

Clinical:
1. Metastatic bone tumor, primary lesion undetermined.
2. Fracture, pathological, shaft left femur, upper third ununited, with shortening.
3. Pathological fracture left mandible.
4. Arthritis not found.
5. Otitis media, residuals of, old suppurative, left, mild.
6. Rhinitis, chronic, hypertrophic, mild.
7. Sinusitis not found.
8. Astigmatism, hyperopic, mild bilateral.

Anatomical:
1. Teratoma of left testicle with metastasis to lymph nodes, stomach, pancreas, kidneys, thyroid and osseous system.
2. Lobular pneumonia.
3. Pyonephrosis, bilateral.
4. Ulcers, gastric, multiple due to 1.
5. Obstruction common bile duct due to 1.
6. Myocarditis chronic.
7. Pleurisy, chronic, fibrous, left.
8. Ulcers, decubital, sacrum.
9. Scar, right inguinal region.
10. Scars, left pulmonary apex.
11. Inanition.

*Treatment.* 36,000 mc-hr. radium cannon to right shoulder two hours daily; 24,000 mc-hr. radium cannon to left pelvis and femur two hours daily; 923 r deep roentgen therapy to left mandible.

*Prognosis.* It was not until February 27, 1935, that the patient complained of pain in the left testicle. On examination a firm, slightly enlarged testicle was noted. Prior to this ex-

amination no pathology referable to the testicle could be found. On April 11, 1935, a great deal of pain in the left mandible with swelling revealed by roentgen examination a pathological fracture. A biopsy from a tooth socket at this time revealed squamous cell carcinoma. Shortly before death, gastric distress with nausea and vomiting developed, with severe anemia, lobular pneumonia and pyuria.

*Cause of Death.* Teratoma of left testicle, with metastasis to thyroid lymph nodes, stomach, pancreas, kidneys and skeletal system. Pneumonia, lobular, right. Squamous cell carcinoma left mandible with pathological fracture.

SUMMARY

Two cases of skeletal metastasis in teratoma of the testicle are presented.

# THE GROSS MORPHOLOGY OF CERVICAL CANCER IN RELATION TO ITS CURABILITY*†

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AMONG the numerous perplexing aspects of cervical carcinoma is the question of the response to treatment. The most important feature of the lesion in this respect is the degree of clinical advancement. Yet this can be determined accurately only in the very early local growths and in the very extensive or far-advanced cases. For this reason, other variable factors assume much importance. Among these are the age of the patient, the type of treatment, the histology of the growth and the gross morphology of the lesion.

Before the advent of radium therapy, the gross morphology of the lesion was deemed important as an indication of the probable extent of the cancerous invasion. Thus cancers which appeared to be frankly cauliflower or everting types were thought to have invaded the adjacent tissues to a lesser degree than smaller cancers which were frankly inverting. By the time it was known that the parametria might be soft to the touch and yet be invaded by cancer, or hard from infection and relatively free of cancer, and that all cancers both invert and evert in the same tumor as they grow, the profession had become so interested in Schottländer's theory of the relationship of histological picture of the cancer cell and clinical cure that it forgot about Winter's morphological classification.

The clinic in which I work has never been able to establish an intimate relationship between the cell type and the curability of the cancer, but has been most interested in any and all factors which help determine the extent of invasion adjacent to the tumor. For this reason, I became interested in the relationship of the morphology and the curability of the tumor, wondering whether the old theory had any value. I find the subject has attracted very little recent attention. Only Graves, Boyd, Norris, and Lynch and Maxwell seem to mention it at all.

Graves[2] states that "the cauliflower type of growth is less treacherous than the infiltrating form, as it gives earlier warning of its presence by bleeding." Lynch and Maxwell,[4] in referring to cauliflower forms, observe that "in the early stages the cancer is purely local and since it expends the greater part of its energy in growing into the cavity of the vagina, it is not malignant in the sense that the inverting growth is." Boyd[1] remarks that "cancer of the cervix may extend on the surface forming a large, fungating, cauliflower-like mass which projects into the cavity of the vagina. This variety usually arises from the lip of the external os, and shows little tendency to invade the deeper tissues. It is, therefore, of limited malignancy, although alarming in appearance. Cancer of the cervix may extend deeply in the direction of the internal os, causing enlargement of the cervix as a whole and eventually producing a deep, ragged, crateriform cavity, lined by crumbling, sloughing debris which bleeds at touch. This is the commonest and, at the same time, the most malignant form."

Even at the present time, I feel that for practical purposes, at least to some degree, we can divide cervical carcinomas into everting and inverting growths according to their relationship to the cell layers from which they spring—even though, at the onset and to an uncertain degree thereafter both eversion and inversion occur at the same time and in the same cancer. The cauliflower type and the rarer, and more frankly polypoid masses which spring from a narrow base and nearly fill the vagina

* The study is made possible by the Cancer Fund of the University.
† Read at the Twenty-third Annual Meeting, American Radium Society, San Francisco, Calif., June 13–14, 1938.

represent the greatest degrees of eversion. The crater-like lesions signify the greatest degree of inversion. Yet difficulties arise in even this simple classification. Cauliflower masses may have sloughed away before the patient has applied for treatment, in which event we can only assume that the lesion probably had been everting, although we cannot gauge accurately the probable depth of invasion of the underlying cervical tissue.

An inverting growth usually gives no symptoms until it invades sufficiently deep to destroy circulation and there is actual sloughing. The everting and especially the cauliflower types bruise easily and give bleeding as an early symptom; because the cancer expends most of its energy in growing into the cavity of the vagina it would seem less malignant than the inverting growth. Norris,[5] in discussing the radiosensitivity of cervical carcinomas, states that "In general, papillary tumors are more sensitive than are those of the infiltrating type . . . Neoplasms that are soft, friable, highly vascular, and of the so-called papillary or cauliflower type usually undergo marked primary regression, and disappear rapidly under suitable irradiation." While our Clinic agrees in general with this statement we have not found that the polypoid forms are as curable as they are said to be, possibly because a growth which plugs part of the vagina is subject to more trauma than one which extends down a shorter distance. Constant trauma may enhance malignant tendencies and stimulate invasion of tissues Even normal activities cause marked trauma to a polypoid mass. Walking, bending, coughing, straining at stool, coitus, etc., all produce trauma of considerable degree. Attempts at reducing the size of the growth by cauterization or dissection at time of treatment causes trauma whose influence is unknown. Certain it is, however, that if the projecting mass is not removed, radium applied in the vagina will lie at considerable distance from the upper advancing edges of the growth which lie in the tissues beneath the base of the cancer; nor are there indications during the few years we have used deep roentgen rays in these cases that the situation has been greatly improved.

I have studied 346 proved cases of carcinoma of the uterine cervix and have grouped them according to the morphology of the tumor. All cases were treated prior to January, 1933, by the Gynecological-Obstetrical Service of the University of California Hospital by radical surgery, with or without radium, and since 1930, by high voltage roentgen rays or radium, sometimes followed by radical surgery. All cases have a continuous follow-up to death, or through a survival of from five to twenty-two years. I have excluded 10 other five-year cures from this compilation because they died as a result of treatment and here I study only those who survived treatment. The excluded patients are as follows: Stage I (Schmitz), 1 case treated by radium; Stage II, 4 cases treated by radical surgery and 1 case irradiated; Stage III, 4 cases treated by radium.

For the past twenty-two years, the cases have been grouped by a single person, thus removing some of the elements of individual variations in classification. Ninety-three, or 26.9 per cent, of the cases were classified as everting and 253, or 73.1 per cent, as inverting. Comparisons have also been made between the two groups according to five-year clinical cures. To permit comparison of the two forms according to the estimated clinical stage of the disease, the cases are divided according to Schmitz' classification. Some cases grouped as Stage I may have had tumors slightly more advanced than those which Schmitz described. The results are shown in the following charts:

Figure 1 represents a five-year survival curve for 16 irradiated cases classed as Stage I. At the end of five years, 87.5 per cent of the patients with everting lesions were alive and free from recurrence while only 75 per cent of the patients with inverting growths were in similar condition.

I am somewhat hesitant in presenting charts for Stage I cases since theoretically

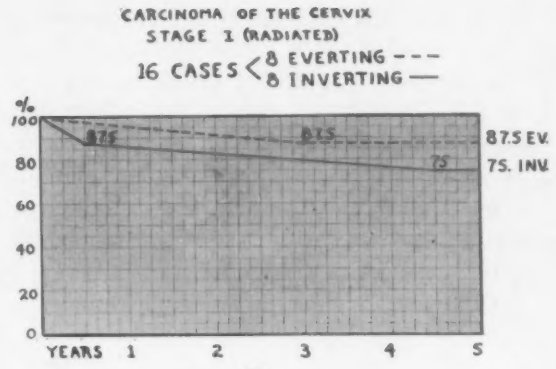


Fig. 1

these represent purely local growths and have not given metastasis. For this reason, there should be no difference between everting and inverting forms for this early group. It is interesting, however, that no Stage I case, which was operated upon radically, has yet died with metastasis, but 2 irradiated Stage I cases died within the five-year period, as did another between the five- and ten-year period.

Figure 2 is a similar comparison of Stage I cases without reference to the form of treatment. After a five-year period 89.5 per cent of those with everting growths and 85.8 per cent of those with inverting growths were alive without demonstrable recurrence.

Figure 3 represents a five-year survival curve for the 32 irradiated Stage II cases,

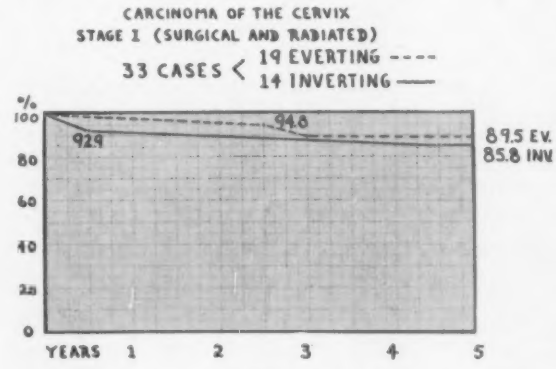


Fig. 2

showing a clinical cure of five years of 50.1 per cent for the patients with everting lesions, and 35.0 per cent for those with inverting growths.

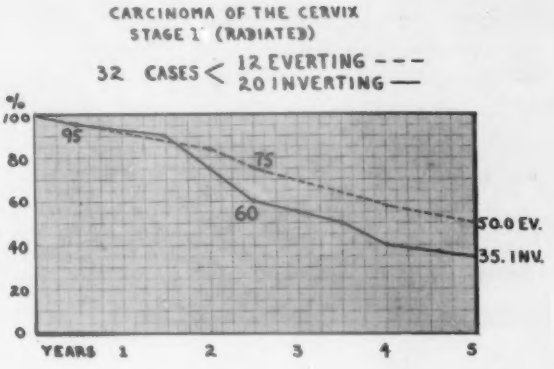


Fig. 3

Figure 4 is a similar comparison of Stage II cases without reference to the form of

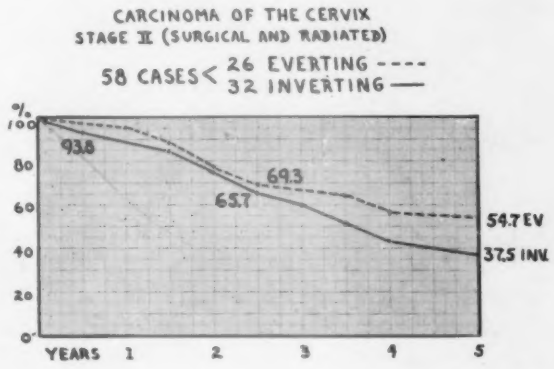


Fig. 4

treatment. After a five-year period, 54.7 per cent of those with everting growths and

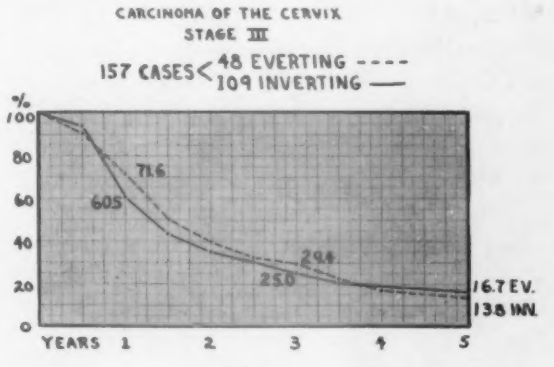


Fig. 5

37.5 per cent of those with inverting growths were clinical cures.

All of the 157 Stage III cases were treated with radium alone or since 1930 also with

high voltage roentgen rays. Figure 5 represents a comparison of the survival curves of the 48 Stage III cases with everting lesions and the 109 with inverting growths. The same general result was obtained. At the end of five years, 16.7 per cent of those with everting lesions remained clinical cures as compared with 13.8 per cent in the inverting group.

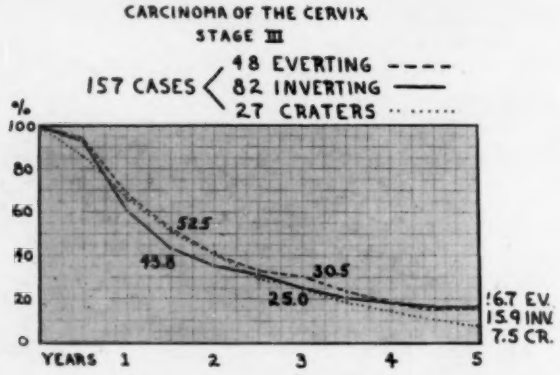


FIG. 6

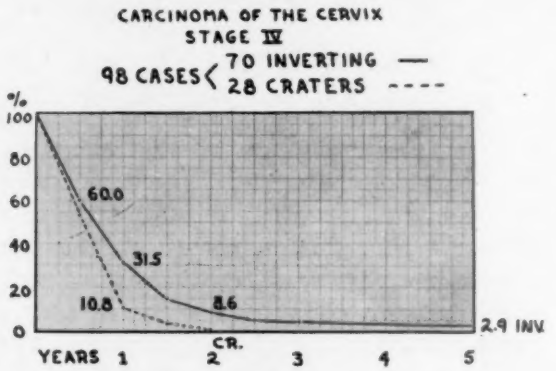


FIG. 7

In Figure 6 the 109 inverting Stage III cases have been divided into 82 cases with simple inverting lesions and 27 with inverting forms that were represented by a crater formation and a comparison made with the 48 cases with everting growths. At the end of a five-year period, 15.9 per cent of the patients with inverting forms and 7.5 per cent of the crater type remain clinically cured as compared with 16.7 per cent of the cases with everting lesions.

Figure 7 represents a comparison of Stage IV cases, all of which are represented by inverting growths, that have been divided into simple inverting forms and craterous lesions. It is observed that none of the patients with a crater type of lesion survived beyond two years, whereas at this time 8.6 per cent of those with simple inverting lesions were still living, and of the latter 2.9 per cent survived for five years.

While an analysis of this small series of 346 cases of cervical carcinoma does not allow definite conclusions, it is of interest because, irrespective of the extent of anatomical invasion, there are more cures in the everting than in the inverting forms, and of the latter, the craterous lesions offer the poorest prognosis.*

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* For discussion see page 76.

Vol. 41, No. 1

# SURVEY OF TWO HUNDRED AND NINETY-THREE CASES OF CANCER OF THE CERVIX UTERI, TWO HUNDRED AND TWENTY-THREE OF WHICH WERE TREATED FROM 1916 TO 1933 BY RADIATION THERAPY AT GRACE HOSPITAL, DETROIT*

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WE PRESENT herewith a survey of a series of cases of carcinoma of the cervix uteri treated in the Department of Radiology of Grace Hospital during seventeen years previous to 1934, together with a few remarks on the statistical conclusions.

The number of cases presented in this paper is so limited and the factual details so incomplete that we are unable to draw any very scientific deductions. A study of these cases, however, together with thirty-four years' experience in treating cancer by radiological methods may perhaps justify some observations we make concerning carcinoma of the cervix uteri.

In spite of the vast amount of research in cancer centers and laboratories for animal experimentation, there is still a great dearth of knowledge concerning the biological normal and abnormal mechanisms, especially in their chemical and electrical aspects, in the development and decadence of neoplasms in people of ever varying constitutions, so that statistics on the value of different methods of treatment fail to give a very correct idea of how and why certain changes have taken place after radiation therapy.

The present plan of classification of cervical carcinoma into stages of growth and development is most difficult of accurate application and open to criticism as a standard for diagnosis and prognosis because the personal factor enters in too strongly. We feel that the grouping we present in our brief tables is very unreliable chiefly because it has been done by several individuals whose ideas vary as to what signs constitute a particular group. And even if the examinations were done by one individual who may be recognized as an expert, we believe his diagnosis would still be unreliable. Is the sense of touch keen enough to indicate whether or not invasion of the broad ligaments has taken place? We doubt it in the early stage of such invasion. Can the earliest stage of development in cancer of the cervix itself—say the stage in which the Schiller test is said to be effective—be recognized by palpation? Should we not designate as Stage III those cases that exhibit inverted or everted ulceration or hard stony nodules in the cervix? Until some other means for positive recognition of parametrial malignant invasion is devised, it seems to us that the present system of grouping is, to say the least, misleading, because if the invasion is already in the parametrium in the earliest stage but not yet palpable, the prognosis is almost as unfavorable as if the metastasis were palpable. At any rate it would seem that because of the likelihood of early metastasis and the difficulty of definite recognition of the same that any visible or palpable lesion of the cervix, such as erosion with bleeding, craterized or vegetative ulcer, or hard nodular infiltration, proved by biopsy to be cancer, should be regarded

* Read at the Twenty-third Annual Meeting, American Radium Society, San Francisco, Calif., June 13–14, 1938.

as, and treated as the present Stage III if invasion of one or both broad ligaments is not demonstrable, and Stage IV if such invasion is demonstrable. That means to treat the entire parametrial system for probable metastasis by roentgen rays, radium in sufficient quantities for this purpose being unavailable at present. We believe a far larger number of what should be called Stages III and IV exist in our series than has been indicated in our tables.

A few cases included in this series have had pre-irradiation operations by the Percy soldering iron cauterization and electrocoagulation. Some others have had partial hysterectomy for fibroid, developing cancer of the cervical stump a few years later. The number of cases in this class is too few from which to draw conclusions. One case had a total hysterectomy following radiation therapy.

In presenting these statistics, we have considered only the cases referred to the Department of Radiology for treatment. Up to the year 1937 the series comprised a total of 293 cases, and this total will be used only in discussing historical data other than therapy, but of course in evaluating the outcome of the treatment only those cases treated prior to 1933 will be considered. The cases then up to 1937 were divided as follows:

*Type of Cases*

| | |
|---|---|
| Cervical carcinoma | 259 |
| Carcinoma of the cervical stump after supracervical hysterectomy for fibroid | 9 |
| Recurrence after operation | 18 |
| Recurrence after roentgen rays and/or radium elsewhere | 7 |

In considering the stage or extent of involvement, we have used the familiar League of Nations classification, dividing the cases into four stages as follows:

*Extent of Involvement*

| | |
|---|---|
| Stage I | 36 (13.4%) |
| Stage II | 31 (11.8%) |
| Stage III | 35 (13.3%) |
| Stage IV | 161 (61.5%) |

The age of incidence varied considerably, the predominating decade being the fourth. Our youngest patient was twenty-three years of age and our oldest eighty-one.

*Age of Incidence*

| | |
|---|---|
| 20 to 30 years (inclusive) | 13 (4.9%) |
| 31 to 40 years (inclusive) | 69 (25%) |
| 41 to 50 years (inclusive) | 90 (32.5%) |
| 51 to 60 years (inclusive) | 67 (23.9%) |
| 61 to 70 years (inclusive) | 31 (11.2%) |
| 71 to 81 years (inclusive) | 7 (2.5%) |

Using Broders' classification the pathology was distributed in this manner:

*Type of Pathology*

| | |
|---|---|
| Squamous cell Grade 1 | 3 (1.7%) |
| Squamous cell Grade 2 | 15 (9% |
| Squamous cell Grade 3 | 59 (37%) |
| Squamous cell Grade 4 | 33 (16.5%) |
| Squamous cell, not graded | 54 (30%) |
| Adenocarcinoma | 9 (5.2%) |

Perhaps the most interesting phase of any statistical cancer survey is the percentage of so-called five-year cures. In this series we consider as five-year cures those patients living five years after the first treatment.

| | |
|---|---|
| Total cases treated prior to 1933 | 223 |
| Total traced cases | 177 |
| Total five-year cures | 36 (20.4%) |

In only 137 of the traced cases was a biopsy taken, and of the five-year cures 28 had biopsy.

| | |
|---|---|
| Total traced cases with biopsy | 137 |
| Total five-year cures with biopsy | 28 (20.4%) |

It is interesting to note that the percentage of five-year cures in all the traced cases is the same as the percentage in the cases proved by biopsy.

Five-year cures according to the extent of involvement are as follows:

| | |
|---|---|
| Total cases in Stage I | 36 |
| Five-year cures in Stage I | 16 (44.4%) |
| Total cases in Stage II | 31 |
| Five year cures in Stage II | 7 (23%) |
| Total cases in Stages III and IV | 161 |
| Five-year cures in Stages III and IV | 10 (6.2%) |

Tabulating the five-year cures according to the histological cell type we have arrived at the following figures:

Five-year cures in squamous cell Grade 1.. 2 (66%)
Five-year cures in squamous cell Grade 2.. 3 (20%)
Five-year cures in squamous cell Grade 3.. 9 (15%)
Five-year cures in squamous cell Grade 4.. 6 (18%)
Five-year cures in adenocarcinoma..... 1 (10%)
Five-year cures in ungraded squamous cell. 7 (13%)

From these meager figures we may suggest that the cell type is no accurate index of curability. We have long believed that more than one grade of malignancy may exist in the same lesion, depending on whether the central or peripheral portion of the malignancy is removed for microscopical examination. Certainly clinically we have observed some very radiosensitive lesions which were placed by the pathologist in Grade 1, and conversely we have seen a number of supposedly Grade 4 malignancies which have been extremely resistant to radiation therapy.

We shall now consider briefly in outline form the malignancies that developed in the retained cervix after supracervical hysterectomy.

(microscopically proved and unproved), or 4.4 per cent, had squamous cell cancer of the cervical stump.

Five cases of supracervical hysterectomy of the 137 proved cases of cancer of the cervix had squamous cell cancer of the cervical stump, or 3.8 per cent. Meigs[1] states that 13 out of 1,771 supracervical hysterectomies at Massachusetts General Hospital, or 0.73 per cent, had cancer of the cervical stump. There were 45,000 women in the hospital during the same period and 1.6 per cent of them had carcinoma of the cervix. Therefore, he argues that cancer of the cervical stump is less frequent than cancer of the cervix in cases which have never had supracervical amputation of the uterus. He says, however, it is more frequent in women who have had hysterectomy for fibroid than for other conditions. We are unprepared with statistics at this time to discuss this latter aspect of the cancer of the cervix problem, but our figures would seem to indicate that cancer of the cervical stump is

SUPRACERVICAL HYSTERECTOMIES PREVIOUS TO RADIATION THERAPY

| Time since Operation | Age | Pathology | Lived after Treatment | Therapy | Other Treatment |
|---|---|---|---|---|---|
| 1½ yr. | 47 | Squamous cell | 2 yr. 9 mo. | X-ray only | None |
| 5 yr. | 43 | Squamous cell Grade 3 | 11 mo. | X-ray only | Radium by surgeon 4 wk. previously |
| Few mo. | 35 | Squamous cell Grade 3 | *Living* 7 yr. 10 mo. | X-ray and radium | None |
| 5 mo. | 34 | Squamous cell Grade 3 | 1 yr. | X-ray only | None |
| 1 yr. | 42 | Squamous cell | 2 yr. | X-ray | Cauterization |
| 16 yr. | 60 | | 1 mo. | X-ray | None |
| 5 yr. | 54 | Squamous cell Grade 2 | 1 or 2 yr. | Radium | None |
| 6 mo. | 49 | | 3 mo. | X-ray | None |
| 3 yr. | 55 | | 4 yr. | X-ray and radium | None |

Nine cases of supracervical hysterectomy of our 223 cases of cancer of the cervix

of more frequent occurrence than is generally considered, and some of the arguments

against radiation therapy of fibroids of the uterus do not necessarily hold.

This series is too small to judge of the efficacy of surgery or irradiation. All of these cases were early so that these statistics cannot be compared with the cases immediate mortality. Of course morbidity after either surgery or irradiation must also be considered.

The following table lists the cases treated for carcinoma of the cervix by hysterectomy prior to radiation therapy.

TOTAL HYSTERECTOMIES PRIOR TO IRRADIATION

| Time since Operation | Age | Pathology | Lived after Treatment | Therapy | Other Treatment |
|---|---|---|---|---|---|
| 4 wk. | 41 | Squamous cell | 9 mo. | X-ray | |
| 2 wk. | 41 | | 4 mo. | X-ray | |
| 3 wk. | 37 | Cautery—no cancer in specimen | 3 yr. (heart disease) | X-ray and radium | Cautery |
| 9 days | 49 | Squamous cell | 1½ yr. | X-ray | |
| 16 days | 35 | Squamous cell | 16 yr. | X-ray | |
| 3 mo. | 50 | Squamous cell, Grade 2 | 4 mo. | X-ray | |
| 4 mo. | 47 | Squamous cell, Grade 4 | 1 yr. | X-ray | |
| 2 mo. | 51 | | 1 mo. | X-ray (2 treatments) | |
| 8 mo. | 40 | | 3 mo. | X-ray | |
| 1 wk. | 30 | Squamous cell | Not traced | X-ray | |
| 15 mo. | 54 | Adenocarcinoma | 4 yr. | X-ray, 2 series | |
| 1 yr. | 42 | Squamous cell, Grade 2 | 9 yr. | X-ray and radium | Recurrence in vault of vagina |
| 2 wk. | 30 | Squamous cell | 9 yr. | X-ray | |
| 2 wk. | 43 | Squamous cell | Not traced | X-ray | |

treated by irradiation alone, because most of our irradiation cases were advanced. However, this table shows that we can obtain cures in early cases by surgery followed by irradiation. Most of the cases that come for irradiation are not amenable to surgery. In our early cases we show 44.4 per cent of five-year cures, which is about twice the percentage shown in this table. In addition there is no immediate mortality from irradiation alone, while with surgery the patient runs the risk of about 7 per cent

Eleven cases had cauterization of the cervix by the Percy soldering iron method or by electrocoagulation before radiation treatment. One of these lived four and a half years but was not well during this time, one lived two years after treatment. The others lived two or three months to a year.

Two cases under thirty years of age have survived the five-year period—they were both twenty-eight years of age when treatment was begun. One, a Stage 1, Grade 4,

squamous cell carcinoma of the cervix, was referred by Dr. Bruce Anderson. She was given roentgen treatment daily from June 26 to July 15, 1933, by the fractionated protracted technique. Dr. Lester Bauer examined her recently and found her to be perfectly well and free from any evidence of cancer, just five years after beginning treatment.

Another case, aged twenty-eight, began treatment in 1931. She was reported by her referring surgeon, Dr. Joseph Israel, as belonging to Stage III, and the report of the pathologist, Dr. Clarence Owen, was squamous cell carcinoma, Grade 3. The uterus was fixed, and there was much bleeding. She was so anemic that several transfusions had to be given. There was clinically a slight recurrence (no second biopsy) in 1932. She is alive and well at the time of writing this, seven years after the first roentgen series began.

There were 23 cases, proved by biopsy, alive and well five years and longer. Ten other cases, which were not proved by biopsy, lived longer than five years. The following table shows the duration of cure:

| *Years* | *Number* |
|---|---|
| 5 | 1 |
| 6 | 4 |
| 7 | 4 |
| 8 | 5 |
| 9 | 2 |
| 10 | 4 |
| 11 | 1 |
| 13 | 1 |
| 16 | 1 |
| | 23 |

Of 8 cases that lived five years or over but finally died of the disease, 6 lived five years, 1 lived nine years, and 1 lived ten years after treatment. Thus the treatment at least held the disease in check and prolonged life much beyond the period of expectancy, but even after ten years of comparative relief from the disease the patient could not be said to be cured, as one or two relapsed after that length of time.

Of the total number in this survey, 52.4 per cent had roentgen and radium therapy; 42.2 per cent had roentgen therapy without radium; 4.4 per cent had radium without roentgen therapy. Twenty-nine, or approximately 88 per cent, of 33 cases (proved and unproved by biopsy), and treated by roentgen and radium therapy, lived five years and longer. Four such cases, treated by roentgen therapy without addition of radium lived five years and over. None of the 10 patients treated with radium alone survived the five-year period.

Nearly all the cases in this series should, in our opinion, be classed as Stage III, and efficient roentgen irradiation throughout the entire pelvis should have been administered to all of them. Radium irradiation was inadequate.

For some time we have been concerned about the rôle that infection plays in influencing the treatment of carcinoma of the cervix. We are fully convinced that many more cases would be cured if ample time could be taken, say one or two weeks, to prepare the patient for radiation treatment. As pointed out by Regaud several years ago, cancer and infection thrive together. The traumatism of biopsy and of dilatation of the cervix for insertion of radium-carrying tubes, it would seem, would tend to spread infection from the vagina. Clinically we have observed a few very early cases of cancer of the cervix that seemed to metastasize rapidly in the pelvis and up along the ureters very soon after radium insertion in the uterus. Did the radium-bearing tube carry infection up into the fallopian tubes and inoculate the broad ligaments? And did this infection lower resistance against cancer? We have suspected as much. On the other hand, other cases which we thought were handled unnecessarily roughly by the surgeon in dilating the cervix for radium insertion survived the five-year period. These opposite results could be attributed to the variance of virulence of infectious processes and the natural defense against them. Roentgen rays in moderate dosage seem to control many types of infection. They are applied without surgical aid as is necessary in applying radium in the uterine cavity.

Therefore we stress the administration of roentgen therapy in moderate dosage in the beginning before radium therapy.

Naturally we have often asked ourselves the question, why is it that we cure or keep alive for five years or more about 20 per cent of all cases of cancer of the cervix coming to us for treatment and with practically the same apparatus, the same technique we are unable to cure or give much relief to the other 80 per cent? Of course innumerable factors enter into the question, factors that may not be brought to light for several generations. It has always seemed to us that more stress should be laid on the scientific solution of these problems than on so much "educating the public" concerning cancer. We really know very little about the etiology and consequently the prophylaxis of cancer. As the years go by, we sometimes have to right about face and tell the public a different story, thus weakening their faith in scientific medicine. If more emphasis were laid on regular general examinations, and physicians were better educated for this purpose, including a better knowledge of cancer, there would be less cancerophobia and there would be more early cases of cancer brought to the expert for treatment.

*Radium Technique.* We have followed a slightly modified Regaud technique since 1925, using 1.5 to 2 mm. platinum screens and distributing the radium in the cervical and uterine cavity and in the vaginal pericervical areas. An average of 4,000 to 6,000 mg-hr. in three or four days has been given after roentgen irradiation. Occasionally radium has been used first but against our best judgment. Previous to 1925 we used radium more often at first and in a brass tube with 1 or 2 mm. walls, 50 mg. for twenty-four to forty-eight hours.

*Roentgen Technique.* In 1922 we used a modified Seitz-Wintz technique about as follows: 200 kv., 1 mm. Cu and 1 mm. Al, 5 ma., 50 cm. distance, 100 to 110 minutes on each of 4 successive days. Of course we were not measuring in roentgens in those days. We were using 5 ma. air-cooled Coolidge tubes which varied much in vacuum because of changes in external conditions, thus varying the voltage and output of the tube. We now figure we could then scarcely get a maximum 4 r per minute on a 20 by 20 cm. field and probably not more than 3 r per minute. So in 110 minutes we would give say 330 to 440 r. In four days the patient would receive not more than 1,320 to 1,760 r and the treatment was completed, but the latter figure is a good dose for four days. Frequently nausea, vomiting and diarrhea followed.

By 1924 we were using a water-cooled 30 ma., 200 kv. tube and a new transformer. We then treated on three or four successive days at 50 cm. distance, filtered with 1 mm. Cu and 1 Al, giving what we now calculate was about 400 r per day (with back-scatter) for four days—a total of about 1,600 r.

In 1927 we were still following this technique with a little increase in dosage.

Early in 1928 we began treating by the saturation technique of Pfahler, treating our cases daily for about three weeks. This was continued until 1933, since which time we have followed more or less the techniques suggested by Regaud and Coutard, and have treated our cases daily from three to five or six weeks with roentgen rays and followed with radium.

For a long time we have felt that in some cases of cancer, gamma radiation was of greater value than roentgen rays, not so much because of the difference in wave length as because of the more continuous irradiation possible with radium and not practical with roentgen rays. But Mottram[2] has experimented with gamma radiation on roots of beans and transplanted mouse tumors. He found that with thirty minutes' exposure given twenty-four hours apart for seven days (521 r total), 73.3 per cent of the tumors disappeared, while if practically the same sized dose (525 r) were given at one time continuously in 210 minutes, only 27.7 per cent disappeared and some of them grew more rapidly until they threatened the life of the animal. The tumors treated by a spaced technique melted

away very rapidly during the twenty-sixth, twenty-seventh and twenty-eighth days. He pointed out that if the whole seven-day dose were given at once ($3\frac{1}{2}$ hours), the irradiation is going on, while metabolism and growth are presumably not active because mitoses practically ceased after the second thirty minutes' exposure.

This experimentation suggests then that continuous irradiation is much less effective than spaced irradiation. Should radium applications then be made to the cervix only a short time once in twenty-four hours for several days? Or should some method of periodic irradiation after the plan of Coutard be attempted?

Of course these experimental findings may not, and probably do not, apply to all tumors whose metabolism and growth as measured by mitoses vary considerably. Mottram therefore says that for large doses spacing should be wide, and for small doses, narrow. We have had some success in metastatic carcinoma of the neck with daily gamma irradiation fifteen to twenty hours a day (interrupted for care, meals, rest, etc.) over a period of two weeks, giving from 30,000 to 50,000 mg-hr. in that time. In many of them the tumors have improved greatly and disappeared for a few months to longer than five years, but in the majority of cases fatal relapses have taken place. Would we have done better with regular and wider spacing as suggested by the work of Mottram? The Stockholm and other clinics for many years have included a wide spacing it might be well to imitate more generally.

However, we are of the opinion that the goal we have been aiming at so long in cancer therapy should not be just the removal or destruction of cancer cells. We cannot do either without sacrificing or damaging a goodly number of normal cells whose function is to differentiate for work for the organism as a whole. Is it possible that in our surgery or radiation therapy we are sacrificing important cells which have defensive if not actual anticancerogenic functions? Indeed, while we may not prove this as yet, we know that the function of normal cells is to grow up, so to speak, and in that evolutionary process to build up and supply that which is necessary for the healthful operation of the organism as a whole, while the cancer cell does not differentiate with functions of a normal cell but is destructive to the normal cells and the organism as a whole. So it would seem that greater efforts should be made to strengthen and preserve the normal defense.

Reimann,[3] in discussing the biology of the cancer cell says, "It is perhaps better to stress less the individual cell than the fact that the protoplasm of cancer, even though it does differentiate into cells, fails to differentiate as does the protoplasm of normal cells, and fails utterly to organize as a whole."

## SUMMARY

We have presented several tables of statistics concerning 293 cases of carcinoma of the cervix, 223 of which were treated by radiation therapy prior to 1933.

In our list of 223 cases up to 1933 we find 9 cases of carcinoma of the cervical stump after supracervical amputation for fibroid tumor, that is 4.4 per cent, or deducting the cases unproved by biopsy there were 5 cases, or 3.8 per cent, of squamous cell carcinoma in cervical stumps.

All cases as they came were accepted for treatment, and figure in our statistics. About 75 per cent were far advanced. Of the 223 cases, 137 were proved by biopsy and 20.4 per cent of these were cured for five years or over, that is 20.4 per cent of the "run of mine" cases. This percentage of five-year cures in 177 traced cases comprising both those histologically proved and those only clinically diagnosed is identical with that of the biopsied cases.

Broders' grading was used in nearly all biopsied cases. It appears that at least some tumors with a low grade of malignancy are radiosensitive while many of those with the higher grades are not.

Eleven cases which had cauterization by the Percy soldering iron or by electrocau-

tery previous to irradiation did not live through the five-year period.

Fourteen early operable cases had panhysterectomies at varying intervals before radiation treatment. Three of these, microscopically proved, lived beyond the five-year period—2 for nine years and 1 for sixteen years.

Two cases of squamous cell carcinoma, each twenty-eight years of age, who had radiation treatment alone have survived the five-year period—1 for seven years.

Twenty-three cases, proved by biopsy, recently traced are alive, well, and clinically cured after five, six, seven, eight, nine, ten, eleven, thirteen, and sixteen years.

Comments are made on the facts brought out by the survey.

In conclusion, our series is a small one for distribution over so many years during which radiation apparatus and technique have undergone numerous changes. Surgery also of different types and time of performance with relation to the radiation therapy of some cases in the series has varied. The methods of diagnostic precision are also limited. While these factors combine to make a study of this kind of limited scientific value, we think we have gained some knowledge from it which will prove of practical value in the future treatment of carcinoma of the cervix uteri.*

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* For discussion see page 76.

# THE SIGNIFICANCE OF UROLOGICAL SURVEYS IN CERVICAL CARCINOMA*

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ACCORDING to Ewing,[5] "The natural termination of most cases of uterine cancer is through uremia from occlusion of the ureters." As far back as 1858, Wagner[13] noted in a large series of autopsies of cervical carcinoma that "many of the women were quite fat and failed to show the wasting commonly associated with advanced malignant disease." He found that marked ureteral dilatation was present in one-third of the cases and that only a few had metastases in distant organs. In 1893 Winter[15] conducted a similar study and reached the same general conclusion. In 1895 Williams[14] reported a study of 78 autopsies of cases of carcinoma of the cervix uteri. In this series he noted extensive renal disease in every instance, with hydronephrosis and hydroureter in 86 per cent and distant metastases in only 20 per cent. He observed that death was usually caused by ureteral blockage rather than by the infiltration of carcinoma.

Since the use of roentgen and radium therapy, further studies along clinical as well as pathological lines have been conducted with similar observations. In 1926, Herger and Schreiner,[9] reporting 32 autopsies, found gross urinary pathology in 65.6 per cent. In 50 cases of advanced cervical carcinoma checked urologically, the same authors found hydro- and pyonephrosis in 48 per cent.

Behney,[1] Faerber,[6] and Morton,[11] working independently, reached a similar conclusion. In 166 autopsies, Behney reported 65 per cent with ureteral obstruction and hydronephrosis. It is significant that 58 per cent of the irradiated cases (80 cases) and 72 per cent of the untreated cases (86 cases) showed ureteral dilatation. In 150 autopsies, Faerber found ureteral pathology in 72 per cent.

In 1934, Everett,[4] reporting 940 cervical carcinomas admitted to Johns Hopkins Hospital, found that 50.3 per cent revealed urinary symptoms on admission.

In 1936, Graves, Kickham and Nathanson,[7] reporting clinical observations on 257 cases, found renal symptoms such as nausea, vomiting, dizziness, headache and visual disturbances in 41 per cent of the cases before treatment, and an additional 24 per cent after treatment, making a significant total of 65 per cent. Blood chemistry revealed nitrogenous retention in 54 per cent of these cases and phenolsulphonphthalein excretion was below 20 per cent in 40 per cent of the cases. Of 87 autopsies reported by the same workers, 79.3 per cent showed hydronephrosis due to ureteral occlusion. Of these 69 cases, 33⅓ per cent showed unilateral and 66⅔ per cent showed bilateral involvement.

## COMPLICATION OFTEN OVERLOOKED BY CLINICIANS

In spite of the work that has been published over a long period of years, few gynecological, urological and pathological texts have given this subject the prominence it deserves. Moreover, we believe that very often in the clinical care of these patients, the gradual occlusion of the ureter with its concomitant symptoms of pain, anorexia, fever, etc., is often overlooked.

Convinced that many of these cases of ureteral obstruction can be greatly relieved if the condition is recognized early and treatment is directed to this complication, we decided in October, 1936, to make a careful urological survey of all patients

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admitted to the Brooklyn Cancer Institute, with the proved diagnosis of carcinoma of the cervix. The examination consisted of blood chemistry, urinalysis, phenolsulphonphthalein test, and a urological examination. These procedures were repeated following radiation therapy and during the years of follow-up.

Our survey has covered too short a period to make more than an interval study at this time. This report is sufficient to show the high percentage of cases admitted with ureteral obstruction and advanced hydronephrosis.

The survey has helped us to recognize the condition early and to realize that the ureteral stricture must be treated actively as by ureteral dilatation, ureteral transplantation, nephrostomy or nephrectomy. The immediate improvement following any of these procedures, when successful, is sometimes remarkable, as reported in a previous paper.[3]

## SYMPTOMATOLOGY

In 1930 Schmitz[12] so ably called to our attention the symptoms of ureteral obstruction that we quote:

> The symptoms are a constant dull and often acute pain in the affected side. It is usually referred to the loin, or to the pelvis, or to the site of obstruction and trauma or to the sacroiliac synchrondrosis. The pain radiates outward into the muscles of the buttocks, downward into the thigh, simulating a sciatica, and upwards to the region of the kidney. Nausea and vomiting may be observed. Disturbances of urination are usually lacking. If infection coexists the patient may experience an initial rigor, pyrexia, anorexia and prostration.

In our experience with moderately advanced hydro- or pyonephrosis, the patient usually complained of anorexia, malaise, occasional chills with fever, and dull or sharp pain, which may be more or less constant, localized or diffuse.

## ETIOLOGY

The etiology of ureteral obstruction is four-fold: (1) ureteral blockage due to an inflammatory parametritis; (2) involvement of the ureteral wall and sheath by carcinomatous infiltration; (3) ureteral obstruction, in a small number of cases, due to a transient edema following irradiation; (4) ureteral obstruction due to post-irradiation fibrosis.

Prior to the era of irradiation, autopsy findings revealed over 75 per cent ureteral obstruction. Recent studies have shown that, in spite of irradiation, the percentage has not changed materially. It has already been noted above that Behney found ureteral obstruction in 58 per cent of treated cases and 72 per cent in untreated cases. However, clinical studies by Graves, Kickham and Nathanson[8] indicate that symptoms of ureteral obstruction appeared in an additional 24 per cent of the cases following therapy, which brought the total up to 65 per cent. It is possible that the apparent increase, as noted above, may not be due entirely to the effect of the irradiation. The same authors state: "We believe that the cause of ureteral obstruction is found in most instances in the encroaching tumor itself." We are unable to reconcile the above views with those of Martin,[10] Schmitz,[12] and Dean,[2] who believe that irradiation fibrosis plays a great part in ureteral obstruction. In view of the limited amount of autopsy material obtained since this study was instituted, we hesitate to draw definite conclusions from our own series. More detailed urological surveys and further studies of autopsy material in a larger number of cases may aid in the solution of this problem.

## TYPE OF RADIATION USED

The theory of our technique in planning radiation dosage has been based on the premise that the usual cause of ureteral stricture is due to the advancing carcinoma and not to post-irradiation fibrosis and resulting stricture of the ureters. The usual cycle of roentgen therapy consisted of six portals, 10×15 cm., two anterior, two posterior and two lateral; treating three portals on each side on alternate days, delivering 200 r in air per area per treatment, a total

of 2,400 r in air per portal. The other factors include 200 kv. pulsating potential, filtration with 2 mm. copper and 1 mm. aluminum and 50 cm. skin-target distance. An additional 1,200 r has often been given to the perineum provided there is involvement in the vagina. Recently an intravaginal cone 2.5 cm. in diameter has been used for an additional 2,000 to 4,000 r, all other factors remaining constant. The estimated depth dose to the center of the pelvis averaged from 5,500 to 6,000 r, and never exceeded 7,000 r.

Approximately one month following the completion of this roentgen cycle, radium therapy was usually instituted. At that time we frequently found not only that the original tumor had disappeared clinically, but also that varying degrees of atresia of the vaginal vault had developed. The radium was applied by tandem to the uterus, and by colpostat and central cork to the vagina. The uterine applicator contained 30 to 40 mg. of radium element (with the minimal dose to the fundus) and was filtered by 1 mm. of platinum and a thin rubber sac. Each vaginal applicator contained 15 to 20 mg. of radium element and was screened by 1.5 mm. platinum and 1 cm. of rubber. When possible, the radium was left *in situ* for 100 hours, giving a total dosage of 6,000 to 7,000 mg-hr. divided between the uterus and vagina. If the temperature rose over 102°F., or other toxic symptoms appeared, the vaseline gauze vaginal packing and radium were removed. Roentgen study of the radium *in situ* has shown that the position of the applicators changed to a considerable degree after an interval of a few days. This lateral shift of the vaginal applicators during the treatment may have been a factor in overirradiation of the ureters. Our usual technique varied with the degree of obliteration of the fornices and the extent of vaginal stenosis. At times only the colpostat could be used and the central cork, which we placed between its arms and against the external os, had to be omitted. In more marked stenosis, we have had to dispense with the colpostat entirely and to employ the central cork alone. The use of interstitial radium was limited to carcinoma of the cervical stump. It is significant to note that only 70 per cent of our cases were able to complete their radiation therapy. In the remainder, therapy was discontinued because of advanced disease or complications.

## STATISTICS OF THE GROUP UNDER CONSIDERATION

In a period of less than two years, over 100 proved cases of carcinoma of the cervix were admitted. Only those cases were excluded whose hospital stay was too short to enable a partial checkup, such as biopsy, complete history and physical examinations, etc. Our records of this group showed that 82 per cent were white and 18 per cent were negro.

The nationalities of the patients represented a typical cross section of admissions to a municipal hospital in a large cosmopolitan city. Only 6 per cent were Jewish.

| | |
|---|---|
| U. S. | 51% |
| Italians | 13% |
| Poles | 5% |
| Germans | 5% |
| Irish | 4% |
| West Indians | 4% |
| English | 3% |
| Austrians | 3% |
| Russians | 2% |
| Swedish | 2% |
| Unclassified | 8% |

The age limits varied from the youngest of 25 years to the oldest of 74 years; the average age was 48 years.

| | | |
|---|---|---|
| By decades | 25–30 | 8% |
| | 30–40 | 18% |
| | 40–50 | 38% |
| | 50–60 | 17% |
| | 60–70 | 17% |
| | 70–74 | 2% |

The average parity was 3 and the largest was 10.

The average gravidity was 4.1 and the largest 15.

Parity 15%— 0 Pregnancies
18%— 1 Pregnancies
20%— 2 Pregnancies
11%— 3 Pregnancies
10%— 4 Pregnancies
6%— 5 Pregnancies
2%— 6 Pregnancies
4%— 7 Pregnancies
3%— 8 Pregnancies
3%— 9 Pregnancies
5%—10 Pregnancies
3%—no record

On admission, a careful history was taken. The chief complaints were found to be:

| | |
|---|---|
| Vaginal spotting in | 9% |
| Vaginal bleeding in | 81% |
| Pain | 33% |
| Discharge | 15% |

In many cases there were a multiplicity of complaints. The average duration of symptoms prior to admission was 8.85 months.

Clinically the cases were grouped according to the Schmitz classification and their frequency was noted as below:

| | |
|---|---|
| Stage I— | 2% |
| Stage II— | 25% |
| Stage III— | 31% |
| Stage IV— | 52% |

Stages III and IV had parametrial extension with the possibility of ureteral involvement.

Pathologically the cases were grouped as follows:

| | |
|---|---|
| Prickle cell carcinoma | 37% |
| Transitional cell carcinoma | 55% |
| Anaplastic carcinoma | 4% |
| Adenocarcinoma | 4% |

The associated conditions encountered were:

| | |
|---|---|
| Cardiac | 10% |
| Diabetic | 9% |
| Syphilitic | 7% |

The following complications were found in our series and their frequency noted as follows:

| | |
|---|---|
| Secondary anemia | 44% |
| Pneumonia | 4% |
| Pulmonary metastasis | 4% |
| Edema of legs | 4% |
| Osseous metastasis | 3% |
| Rectovaginal fistula | 2% |
| Intestinal obstruction | 1% |
| Drug addiction | 1% |

(Hemoglobin 50 per cent Sahli and red blood cells 2,500,000)

The bladder findings were:

| | |
|---|---|
| Cystitis in | 59% |
| Elevation of trigone | 30% |
| Ulceration | 6% |
| Vesicovaginal fistula | 4% |
| No pathology | 12% |

Complications associated with the ureters and kidneys were:

| | | |
|---|---|---|
| Right ureterorenal pathology | 23% | Total with renal pathology 52% |
| Left ureterorenal pathology | 10% | |
| Bilateral ureterorenal pathology | 19% | |
| No ureterorenal pathology | 31% | |
| Chart incomplete to determine | 17% | |

In this series, several patients showed early hydronephrotic changes which became progressively worse, as shown by subsequent checkup six months or a year later. This, we partly attributed to the patients' refusal to permit any urological treatment. Some of these patients who refused urological treatment at first returned to us later for amelioration of their condition, at which time their unsatisfactory state precluded any surgery or attempted ureteral dilatation. On the other hand, there was a small number who received early, active therapy plus ureteral dilatation, but who nevertheless showed progressive urological changes. We believe that when untreated these changes are definitely progressive, and that therefore early active urological treatment should be instituted in every case, as this is our only known method of alleviation.

We have found that in the advanced cases where cystoscopy and retrograde pyelography may produce shock, or where it is contraindicated for other reasons, intravenous urography may be substituted,

Fig. 1. Carcinoma of cervix, unilateral hydronephrosis and hydroureter. *A*, Case R. P., intravenous pyelography; *B*, Case M.D., retrograde pyelography.

as it readily shows involvement of the kidney or ureters. The only complications that we have encountered in the intravenous procedure have been a severe chill in some cases that were known to have extensive pyelonephritis.

The complete absence of renal pain or tenderness or any other urological symptom, even in advanced stages, may easily lead the clinician astray. Complete obstruction of the ureter, with no kidney function on the involved side, has been observed by all of us. In making an early diagnosis of this complication we have found phenolsulphonphthalein excretion to be even more reliable than blood chemistry. Retrograde or intravenous pyelography has served best to visualize morphological changes in the kidney pelvis and ureter (Fig. 1, *A* and *B*). The site of ureteral obstruction was usually found to be 4–6 cm. from the vesical junction at the level where the ureters pass closest to the cervix in the base of the broad ligaments.

In several of our autopsies (Fig. 2) which revealed marked ureteral fibrosis and stenosis, a thorough search failed to reveal viable carcinoma cells.

## TREATMENT

Treatment has consisted of routine dilatation of the affected ureters wherever it is possible to pass catheters beyond the area of obstruction. Irrigation of the affected kidney pelvis has occasionally held the infection in check temporarily. When

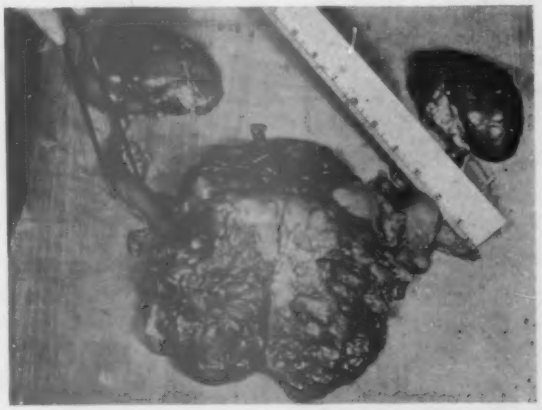

Fig. 2. Gross specimen, carcinoma of cervix, showing bladder dissection with bilateral hydroureter.

the lesion is unilateral and has extended to complete obstruction of one ureter, it is our opinion that nephrectomy is preferable to nephrostomy or any type of ureteral transplantation.

## SUMMARY

1. Ureteral obstruction is the most frequent complication in cervical carcinoma.

2. This clinical study has confirmed the conclusion as to the high percentage of ureteral obstructions in cervical carcinoma, namely 52 per cent. This may be due to:

(a) An ascending infection extending to the parametrium or peri-ureteral structures.

(b) To the tumor itself involving the ureteral wall or encroaching on the adjacent structures.

(c) To a transient edema following irradiation.

(d) To replacement fibrosis, post-irradiation.

3. Considering the frequency and the gravity of this complication, we feel that every case of cervical carcinoma should have a urological survey made upon admission, after completion of treatment, and at intervals as indications may arise.

4. The condition is definitely progressive and leads to death through infection, uremia, or both.

5. Partial ureteral obstruction has not been considered a contraindication to radiation therapy.

6. Treatment should consist of ureteral dilatation when possible. Nephrectomy, ureterostomy, and ureterosigmoidostomy have their indications, and, in some instances, may have definite value in saving life. In complete unilateral ureteral obstruction, we emphasize the value of nephrectomy.*

This review was made possible by the cooperation of the Urological and Gynecological Services of the Brooklyn Cancer Institute. We acknowledge the assistance of our pathologist, Dr. Herman Bolker, in placing biopsy and autopsy material at our disposal. We would also like to thank Dr. Sidney F. Auerbach for his help in summarizing the material for this paper.

* For discussion see page 76.

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# THE MANAGEMENT OF MAJOR COMPLICATIONS DURING RADIUM THERAPY OF CARCINOMA OF THE CERVIX*

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THE broken-dose method of radium treatment of carcinoma of the uterine cervix has been employed at The Mayo Clinic for many years. By the use of this technique, therapy may be individualized. However, a complete initial treatment for the average Stage III lesion ordinarily consists of approximately 7,000 millicurie-hours, given in eight applications in a period of three weeks, distributing the radiation as homogeneously as possible throughout the cervical canal, fundus of the uterus and vaginal walls. We feel that this is the safest and most effective method of treatment and is associated with the lowest morbidity and mortality.

In as serious a disease as cancer of the cervix, which is usually first seen in an advanced stage of development, major complications may be expected in a certain percentage of cases, especially when these patients remain under observation for a period of weeks. All carcinomas of the uterine cervix are infected when first seen. Infection usually is eliminated by the use of douches and by the application of antiseptics at the time of each application of radium. Avoidance of trauma in the course of administering treatment helps to forestall spread of infection. The radium treatments are applied under direct vision when the patient is in the knee-chest position. However, even with the maximal amount of care, in a small percentage of cases infection may spread to produce pelvic cellulitis, peritonitis or septicemia. The latter is one of the serious complications requiring expert management.

The other frequent, serious complication is hemorrhage. Cancer, growing without restraint, erodes blood vessels in its path and fatal hemorrhage may ensue. Toward the conclusion of the course of radium treatment this complication is not often encountered; the effect of treatment in stimulating the replacement of malignant cells by growth of connective tissue serves as a protection.

Naturally, more is learned by study of difficult cases associated with special problems than by analysis of the average lesion which responds to treatment without incident. Consequently, it seemed worth while to review the serious complications, their management and the results obtained during the past year, especially because a new drug, sulfanilamide, has been in use during the latter part of the year and is on trial now in respect to its merits in combating these serious types of infection.

During 1937, 117 patients who had carcinoma of the uterine cervix were treated with radium. Most of these patients had advanced inoperable lesions when first seen. This has been the usual finding in past years. Ninety-five patients, or 81 per cent of the total, were classified as Stage III or Stage IV as regards the anatomic extent of the growth.

During their course of treatment, 8 of the patients, or 6.8 per cent of the total, experienced a serious complication necessitating that radium treatment be abandoned. Of these 8, one patient succumbed to the complication, yielding a mortality of 0.9 per cent or 12.5 per cent of the group with serious complications. The youngest of these 8 patients was thirty-two years of age, the oldest sixty-six, and the average age was forty-six years. Analysis of these 8 patients who had serious complications indicated that all had advanced lesions.

* Read at the Twenty-third Annual Meeting, American Radium Society, San Francisco, Calif., June 13–14, 1938.

Two were classified as Stage IV, 1 as Stage IV modified, 4 as Stage III and 1 as Stage III modified. The term "modified" means that the lesion had been altered by previous treatment elsewhere. Biopsy of the malignant growth disclosed squamous cell epithelioma, Grade 4, in 3 instances; squamous cell epithelioma, Grade 3, in 4 instances; and adenocarcinoma, Grade 3, in 1 instance.

Previous to 1937, before the use of sulfanilamide, the management of serious infections consisted mainly of discontinuing the applications of radium; rest in bed; hot douches of sodium bicarbonate; the application of heat or cold to the pelvis; increasing the intake of fluids; administration of acetylsalicylic acid and quinine to reduce temperature, and drainage of the uterus if pyometritis existed. Examination of the blood, vaginal smears and cultures, blood cultures, and the sedimentation rate furnished valuable guides to further treatment. Examination of urine obtained by catheterization and determinations of the concentration of blood urea yielded valuable information regarding the function of the kidneys. Administration of glucose solutions intravenously was of value if fluids were tolerated poorly by mouth.

The management of vaginal hemorrhage has been unchanged in recent years. Immediate packing of the vagina tightly with gauze, applied when the patient is in the knee-chest position, which permits full expansion of the vagina for adequate packing, is the first step. However, this packing should be changed daily or damage to the vaginal mucosa soon will become manifest. Frequently, a vaseline sponge is inserted over the bleeding region ahead of the vaginal pack and is left in place for forty-eight hours, or longer, as this minimizes the injury to the delicate mucosa. Supplementary measures are application of ice bags to the pelvis, inducement of rest by hypodermic administration of morphine, elevation of the foot of the bed and transfusions, if they become necessary. Radium applied at a distance over the spleen has proved of value in arresting hemorrhage. Also, pelvic radium treatments are continued because the gradual shrinkage of the tumor and stimulation of the growth of connective tissue produce in themselves a hemostatic effect. Frequent blood counts and determinations of the value of hemoglobin are requisites and early blood grouping for transfusion is essential.

The major complications during 1937 among 8 patients were distributed as follows: 4 patients had pelvic cellulitis, 2 had pelvic cellulitis with hemorrhage, 1 had hemorrhage combined with cerebral accident and 1 had hemorrhage and uremia. Each of the last 2 patients mentioned had pneumonia as an additional complication. Also, a vesicovaginal fistula occurred in 1 case in which the lesion had been modified by previous treatment. Hence, 6 of the 8 patients had a serious degree of pelvic cellulitis which was combined with hemorrhage in 2 instances. Sulfanilamide was not introduced as a therapeutic agent until the spring of 1937; thus, only 3 of these patients had the benefit of this form of therapy. The 5 patients encountered earlier in the year received the therapeutic measures outlined above and all improved gradually. The temperature became normal in all cases and the patients returned to their homes.

Later in the year, 3 desperately ill women did receive undoubted benefit from sulfanilamide therapy. A fever of 102 to 103°F. (38.8 to 39.4°C.) suddenly developed in 1 case and examination of vaginal smears gave evidence of a green-producing streptococcus. Organisms were not found in the blood. Sulfanilamide therapy was started in the accustomed dosage of 15 grains five times a day for a week, and then in gradually lessened dosage as improvement occurred in the next two weeks. Then a blood transfusion was given and after the fever had been absent for several days, the patient was allowed to return home.

A second patient responded more rapidly. Pelvic cellulitis had progressed to pyometritis with daily elevation of tem-

perature to 103°F. (39.4°C.). Following a blood transfusion, 15 grains of sulfanilamide was given four times a day. In five days, her temperature became normal and she was allowed to go home. Two months later, on her return to The Clinic, all signs of inflammation had disappeared and the lesion had responded well to radium therapy. Further treatments were given without incident.

A third patient responded almost immediately to a heavier dosage. Following hemorrhages which reduced the concentration of hemoglobin to 40 per cent (Dare), acute pelvic cellulitis developed and caused elevation of temperature to 104° F. (40° C.) daily. The sedimentation rate rose to 46 mm. per hour. Fifteen grains of sulfanilamide were administered orally every four hours and, in two days, the temperature returned to normal and remained so. Further radium treatment a month later was accompanied by another exacerbation of infection, but was controlled again by administration of sulfanilamide for two days only. She returned to The Clinic three months later, at which time both the inflammation and the malignant disease were well controlled.

We feel that sulfanilamide therapy should be under the control of the internist. The degree of concentration of the drug in the blood and urine should be determined frequently and the dosage of the drug should be reduced or its administration discontinued on the appearance of any toxic effects. If used in this manner with careful supervision, we believe sulfanilamide will continue to be a definite advantage in the treatment of these complications.

The one patient succumbed because of a series of late chronic complications and not because of an acute inflammatory process. This woman, aged thirty-five, came with a long-standing, neglected, cervical cancer. She had experienced several hemorrhages and uremia already had begun to develop. A limited course of radium treatment was outlined to control the hemorrhages but the uremia and secondary anemia progressed. Fluids were forced by mouth and were supplemented with intravenous fluids and blood transfusions. Radium treatment was applied to the spleen. The concentration of blood urea decreased to normal for a time but the relatives wanted the patient to remain in the hospital because her home was in a distant part of the country. Finally, the uremia increased, the concentration of urea mounted to 208 mg. per 100 cc. of blood and terminal pneumonia developed. She died after a three months' stay in the hospital.

## SUMMARY

The divided-dose method of radium therapy for carcinoma of the uterine cervix seems attended with less danger and with a much lower mortality when complications do appear than when other methods of administration are employed.

Of 117 patients treated in 1937, radium treatment was abandoned in eight instances because of serious complications. Pelvic cellulitis and hemorrhage occurred in two cases, pelvic cellulitis alone in four, uremia and hemorrhage in one, and cerebral accident and pneumonia in one. We feel that these acute inflammatory processes are inherent in the disease itself and in the lowered resistance of these patients who have large pelvic cancers. Certainly these acute inflammatory processes are not induced by the treatments directed against the cancer, for if such were true, acute inflammatory processes would occur more frequently; in fact, we are convinced that the radium treatments together with cleansing of the part at each application of radium tend to abort these complications in many instances.

All the patients who had acute inflammatory exacerbations and the one who had cerebral embolism recovered completely and were allowed to go home. The one patient whose complication caused a fatal outcome had a chronic, long-standing condition, and died of uremia, pneumonia and inanition.

In three cases, the acute infectious process occurred after the introduction of sulfanilamide into medical practice. These three had the advantage of treatment with this agent and each one responded to carefully controlled administration of the drug. Results were gratifying and we expect in the future to obtain much needed help in combating these rare but serious complications by the use of sulfanilamide.*

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* For discussion see page 76.

# AIDS TO IRRADIATION IN THE MANAGEMENT OF CARCINOMA OF THE CERVIX UTERI*

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THERE are numerous measures that may be used as aids to irradiation in the treatment of carcinoma of the uterine cervix. The results of treatment should be much better if these measures were carried out according to a definite system.

1. *Acetone for Local Bleeding*

For several years we have used acetone as an aid in the control of local bleeding from the cervix, as suggested by Gellhorn.[3] The acetone may be used before, during or after the actual irradiation. The action of the acetone is purely local, being that of a fixative and hemostatic. The technique is simple but should be carried out with attention to important details. If there is much local tenderness or if the patient is apprehensive, a preliminary hypodermic injection of morphine may be given. The treatment may be given on the operating table or with the patient in bed. With the patient's hips slightly elevated, a short *tubular* speculum is inserted into the vagina, the clots gently sponged away and 30 to 60 cc. of pure acetone poured into the speculum so as to come in contact with the cervix and upper vagina. After ten minutes, the acetone is carefully sponged out without removing the speculum, and fresh acetone is applied. After twenty minutes this acetone is sponged out, the total time of application being thirty minutes. Care should be taken not to permit the acetone to drop on the skin of the vulva as a marked burning sensation is produced. However, this may be relieved by the prompt application of water. This treatment of thirty minutes' duration may be repeated once or twice daily for several days if necessary. If the bleeding is not controlled by the acetone, vaginal packing may be inserted, but this is rarely necessary.

2. *Treatment of Anemia*

Blood counts should be made before and during the course of irradiation and any anemia treated at once.

(a) *Iron.* If the anemia is not marked we usually give the following ℞:

| | |
|---|---|
| Iron and ammonium citrate | 60 gm. |
| Simple syrup | 60 cc. |
| Cinnamon water q.s.a.d. | 180 cc. |
| M. Sig. 4 cc. Q.I.D. | |
| (4 cc. = 1.2 gm. of iron) | |

(b) *Liver.* If there is no improvement in the blood picture in one week one-half pound of liver (either raw or cooked) is given daily. In some cases intramuscular injections of liver extract are used. The dosage given depends upon the preparation that is used. If the usual dose is 2 or 3 cc., this may be given daily for a week and then continued once or twice a week for some time. Occasionally iron and liver are given combined in capsules.

(c) *Blood Transfusion.* If the anemia does not improve promptly after the administration of iron and liver, direct transfusion of blood should be employed. If the number of the red cells is below 3,500,000 and the hemoglobin below 70 per cent, transfusion should be seriously considered before continuing irradiation. These transfusions should be repeated at intervals if necessary.

3. *Treatment of Pain*

(a) *Drugs.* Pain is usually treated first by acetylsalicylic acid, which is sufficient in many cases. If necessary, codeine may be given by mouth, often at the same time as the acetylsalicylic acid. Later codeine or morphine by hypodermic injection may be employed. In the far-advanced cases it is cruel to withhold these drugs as there is no problem of drug addiction.

(b) *Subarachnoid Injection of Alcohol.*

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For severe pelvic pain the subarachnoid injection of alcohol is sometimes employed.[7,11] The technique of this injection is simple and the pain is usually relieved. If the pain returns, the injection may be repeated. There is a slight but definite danger of urinary incontinence after the alcohol injection. Therefore, this method is usually reserved for cases where ultimate recovery seems improbable.

(c) *Presacral Sympathectomy*. Pain in the lower portion of the pelvis may sometimes be relieved by laparotomy and resection of the presacral sympathetic fibers (presacral sympathectomy).[8,13] The results of this operation are good in most instances but the patient is often unwilling to submit to this comparatively simple operation unless definite results can be promised.

(d) *Cordotomy*. Cordotomy performed by a competent neurological surgeon will undoubtedly relieve many of the most severe pains accompanying carcinoma of the cervix.[4] However, this is a major operation and the patients require very specialized postoperative care. For these reasons and because of the poor general condition of most of these patients, cordotomy is seldom employed.

4. *Complications in Urinary Tract*

Complications in the urinary tract are quite frequent after treatment of cervical carcinoma. On this account, for the past three years we have performed *routine cystoscopic* and *pyelographic* examinations, as recommended by Schmitz,[12] on all "staff patients" and on many of the "private patients" *before* treatment is started.

The results of these examinations of untreated patients are shown in the following tables.

77 Patients Examined

| | | |
|---|---|---|
| 1. Normal bladder | 55 | 71+% |
| 2. Bladder wall involved, mucosa normal | 20 | 26−% |
| 3. Bladder mucosa involved by tumor | 2 | 2+% |
| 1. Normal pyelogram | 63 | 82−% |
| 2. Double hydronephrosis | 3 | 4−% |
| 3. Single hydronephrosis | 7 | 9+% |
| 4. Functionless kidney | 5 | 6+% |

These figures at once bring up the question, "What is the incidence of hydronephrosis among people in general?" A partial answer to this question has been provided by Dr. Howard Karsner, who has furnished me the following figures from the Institute of Pathology of Western Reserve University. These figures are based on autopsies from a general hospital service including men, women, and children. Total autopsies from March, 1935, to March, 1938, 1,200. Cases of single hydronephrosis, 3. To this should be added 14 cases of surgical specimens received during the same period, making the total incidence of single hydronephrosis 17. Cases of double hydronephrosis, 8. These figures are simplified in the following table:

Autopsies—1200

| | | |
|---|---|---|
| Single hydronephrosis autopsies+surgical specimens | 17 | 1.4% |
| Double hydronephrosis | 8 | 0.6% |

Even with the deductions suggested by these figures, the incidence of hydronephrosis (as well as other complications in the urinary tract) is sufficiently high to justify the continuance of these routine pre-irradiation examinations.

In some cases a ureter obstructed by the pressure from a cancer involving the broad ligament may be dilated by the insertion of a catheter through the cystoscope.[6,10] If the relief is only temporary the procedure may be repeated.

If a bladder ulcer develops after irradiation, it is of the greatest importance to have a definite diagnosis by means of a biopsy specimen. If the ulcer is due to spread of the disease, further irradiation may be considered. However, if the ulcer is due to heavy irradiation that the tissues have received, further irradiation will only make matters worse. The need of this accurate differentiation has been emphasized by Dean.[2] Palliative treatment and patience will usually result in the cure of these "late bladder ulcers."

5. *Complications in Intestinal Tract*

Recently, in addition to the pre-treat-

ment examination of the urinary tract, we have performed a *pre-treatment* proctoscopy and also have examined the colon after a barium enema. These cases are too few for the compilation of statistics but the discovery of a rather large benign papilloma on the anterior wall of the rectal ampulla in one case was of interest.

A definite system of management in the cases of proctitis and intestinal irritation after irradiation is of special importance.

If the symptoms are severe the patient is put to bed. In all cases a non-irritating and low residue diet is used and the patient given full instructions in writing. Petrolatum liquidum 15 to 60 cc. once or twice a day is given by mouth. The larger doses are used if constipation is present but some oil is usually given in small doses, even if diarrhea is present. The diarrhea is best controlled by tr. opii. camph. given by mouth. If the diarrhea is slight 4 cc. is given three or four times daily, but if it is severe the medicine is given in 4 cc. doses every one or two hours until the number of bowel movements is reduced. An enema of plain warm water is usually given once or twice daily even when there is diarrhea.

It is surprising how many patients who appear to be on the verge of intestinal obstruction, clinically and on roentgen examination, clear up permanently on this regimen.

If benign stricture develops it may be relieved by operation. The type of operation depends on the local lesion and on the general condition of the patient. The intestine may be short circuited around the stricture or the involved portion of the intestine may be resected either with or without a preliminary colostomy.[1,9]

## SUMMARY

1. Acetone, applied locally, is an aid in controlling hemorrhage.

2. Anemia may be treated by iron, liver extract and by direct transfusion of blood.

3. Pain may be treated by drugs by mouth or by hypodermic injection, subarachnoid injection of alcohol, presacral sympathectomy, and by cordotomy.

4. Routine pre-treatment cystoscopy and pyelography are advocated. Statistics of a series of cases where this was done are given. Biopsy is essential in the diagnosis of "late bladder ulcer."

5. Routine pre-treatment proctoscopy and roentgen examination after a barium enema are advocated. The management of intestinal and rectal sequelae of treatment is outlined.

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## DISCUSSION OF PAPERS BY DRS. HOFMANN, STEVENS AND PAYNE, HOWES AND STRAUSS, BOWING AND FRICKE, AND POMEROY

DR. ZOE A. JOHNSTON, Pittsburgh, Pa. I have been observing the results in the treatment of carcinoma of the cervix and uterus since 1916. The progress made has been interesting. It does seem that those of us who have small private practices are not the ones to talk about the subject, because it takes a wealth of material to be able to draw any conclusions. Therefore, we depend upon the large clinics for guidance as to the best way to treat these cases. These presentations have been very interesting. I hope that we will be able to draw valuable conclusions from the statistics shown.

Most of us here believe that the combination of radium and roentgen radiation gives these patients the best chance for life. When one person depends almost entirely upon radium, for instance, as Dr. Skinner does, and another depends mainly on roentgen rays, as Dr. Schmitz does, it is difficult to draw conclusions for our own work. There ought to be a balance between the two agents, or a combination of them, which is better than either agent alone. Dr. Arneson's work on calculating a predetermined amount of radiation for these cases, using both agents, seems to me to be a step in the right direction.

In talking about complications, there is one that has not been mentioned. You are all familiar with the article published a few years ago in reference to fractures of the neck of the femur, following irradiation of the pelvis. Our reaction to this was the same as yours. We thought that this did not occur. However, if you look for these cases you will find them. We found our first case this past winter. I do not want to go into the history, but will be glad to give it to anyone interested. Four lantern slides have been prepared to show the progress of this case. I would appreciate having the essayists discuss this complication.

DR. H. H. JAMES, Butte, Montana. I wish to confine my remarks to treatment of cancer of the cervix. I think that you have all had similar experiences to mine, namely, that quite frequently a woman comes into the office with an inoperable recurrent cancer of the vagina, etc., who has previously had a hysterectomy for cancer of the cervix. I believe it was Halsted who once said that it would be a great day for surgeons when all malignant disease was removed from the field of operation. That day bids fair to be at hand, especially in certain cases of cancer, namely, cancer of the cervix.

As statistics show, in the treatment of cancer of the cervix, combined radium and deep roentgen therapy far exceeds any other type of treatment, and I believe that the medical profession of the country should be educated to the fact that cancer of the cervix is largely a problem for irradiation.

Regarding the treatment of cancer of the cervix, I would like to ask Dr. Bowing if he routinely treats the patient by deep roentgen therapy first, and then the vagina and the uterus with radium, or if he first treats the case with radium and then afterwards with deep roentgen therapy.

DR. H. J. ULLMANN, Santa Barbara, Calif. One must consider the possibility that, at times, when what appears to be a Stage II does not respond to treatment as expected, it was perhaps actually more extensive than was determined at the examination. I had a rather unusual opportunity last year to see such a case. A woman in her early thirties came to a County Hospital Clinic with what appeared to be obviously a Stage II carcinoma of the cervix. It had just reached a fornix and there was some lack of mobility. She was scheduled for radium treatment but died of cardiac disease before the treatment was given. At autopsy the local extension was that found at the examination but there was metastatic involvement of retroperitoneal glands well up into the abdomen.

The vaginal pack has always been an interesting subject to me because ordinary gauze frequently causes irritation and becomes very objectionable from the standpoint of odor long before its removal. I tried gauze saturated with petrolatum but the first patient I packed with it unfortunately coughed just as I finished and the whole pack was delivered into my lap. I then changed to iodoform gauze, but in the last year or so I noticed a number of cases of vaginitis at the time of the third radium application and sometimes at the second. At the suggestion of Dr. Sanford Withers, I tried karo corn syrup, which is practically a 50 per cent glucose solution, and found it very satisfactory. No odor develops, it is non-irritating and, important from a clinic standpoint, it is inexpensive. It is sticky and somewhat more difficult to pack than plain gauze, but once placed it and the applicators stay in place. The solution

thins out while the pack is in place and its removal seems less uncomfortable to the patient than that of plain or iodoform gauze.

In order to stimulate discussion on methods of irradiation, I will describe the one I am now using. In the earlier stages of Stage I, where only a small portion of the cervix is involved and no extension demonstrable or suspected, radium alone is used in three applications following closely the technique used at Radiumhemmet. If the entire cervix is involved or there is evidence of the lesion being Stage II, a preliminary course of roentgen irradiation is given. The reason for this is the same one discussed this morning. To produce a preliminary shrinkage due to the lowering of the inflammatory reactions, thus bringing the outer boundaries of the carcinoma nearer to the radium. There is also much less hemorrhage at the first radium placement in the more advanced or fungating carcinoma after thorough roentgenization.

Dr. Charles L. Martin, Dallas, Texas. As some of you know, I have been very much interested in the genitourinary complications of carcinoma of the cervix for the past fourteen years. In 1926 we called attention to the ease with which the ureter may be stenosed with implanted radium. As little as 54 mg-hr. applied to a dog's ureter in monel metal needles produces a partial stricture and a complete blockage results from the use of 75 mg-hr. For this reason, I feel that the insertion of implants into the broad ligaments through an abdominal exposure is a very hazardous procedure and should be carried out with the greatest caution. The better standard techniques using heavily filtered radium in moderate amounts from below do not injure the ureters.

The treatment of strictures is pretty unsatisfactory except in those cases in which the malignancy is completely controlled. When dilatations with metal or wax bulbs do not give relief, I agree with Dr. Pomeroy that removal of the kidney produces the best results.

Dr. Ullmann's use of sticky vaginal packs is characteristic of his ingenuity. We have found it quite desirable to saturate the gauze with a mixture of balsam peru and castor oil. This mixture relieves irritation, keeps down infection and makes it possible to leave a pack in place for several days without untoward results. Many treatments are suggested for radiation proctitis of milder degrees, but the retention of about 3 ounces of olive oil after the use of a small enema has, in our experience, given the greatest relief. I referred to the successful use of sulfanilamide in parametritis complicating cervical malignancy at this meeting last year, but we have since encountered one case in which it was of no benefit whatever. Apparently, only certain types of bacteria will show a favorable response.

The relief of pain in patients suffering from advanced pelvic malignancy is one of our most serious problems. The neurologic surgeon has done a great deal for these unfortunates but in many instances presacral nerve section and alcohol injections have proved unsuccessful in our institution. One must therefore be guarded in making promises before the work is undertaken.

Dr. William P. Healy, New York City. I believe that the physician who is treating cancer of the cervix and has a limited number of cases should have better results than the large clinics, because he can give more individual attention to h's patients. We have too many advanced cases, and we should pay more attention to trying to cure more of our favorable cases and not worry about the hopeless cases. We are doing the best we can with the facilities we have at hand. I think too much time is being wasted on hopeless cases.

When a patient comes in with a cratered cervix, the prognosis is bad by any method of treatment known to us. Yet that patient comes into the group mentioned, because of complications. She probably will have urologic symptoms. It is an easy matter to have a pyelogram made, and, before irradiation of any kind is used, see if there is a poorly functioning kidney on one or the other side; since 75 per cent of the cases are unfavorable, you will be surprised that so many have a kidney that is not working well. This is important, especially if you are going to carry out interstitial irradiation, as has been recommended. If you do not have the preliminary excretory pyelogram showing the dead kidney on one side, you will be inclined to think that your needles did it, when they probably did not have anything to do with it.

I would be very much stimulated if what Dr. Ullmann suggested were done more uniformly throughout the country—preliminary roentgen therapy before radium irradiation. You have no idea of the advantage of cleaning out the infected cervix and obtaining a clean lesion before applying radium.

Dr. Henry Schmitz, Chicago. Alcohol in-

jections or presacral resections should not be done in the presence of pain in the uterus or in the urinary tract.

In about 1,000 cases of cervical carcinoma, only one patient had a metastatic fracture of the femur sixteen years after treatment. We have seen another case or cases due to osteoporosis from irradiation. I feel that this is at variance with the observations in other clinics, but I am stating our actual experience.

DR. H. B. HUNT, Omaha, Nebr. It may be that the unusually high frequency of fracture of the femoral neck following roentgen treatment for carcinoma of the cervix, which occurred at the University of Michigan, results from some peculiarities of their technique. At Michigan two, three, or more pelvic series were usually given to every patient at intervals of two to three months. These repeated exposures may have led to more occlusion of the nutrient vessels than a single course of treatment. The pathologic fractures appear to result from an aseptic necrosis which follows impairment of the local blood supply in the metaphysis of the femoral neck.

DR. WILLIAM E. COSTOLOW, Los Angeles. I want to mention one case we have had in 1,200-odd cases of cancer of the uterus. With a high roentgen dosage, up to a total of 12,000 or 14,000 r, we have had one fracture of the neck of the femur, which occurred two months ago. So far as we can tell from roentgen appearance, it is not due to metastasis. The patient is still in a cast but shows some healing.

DR. HOFMANN (closing). I have nothing to add concerning fractures of the neck of the femur. We have had none, but our series of cases is relatively small. We are still quite enthusiastic about surgery in cases in which it seems indicated, and have been fortunate in having a good five- and ten-year result in those cases treated with surgery. We u e a radium technique similar to that of Dr. Healy, and are now using preliminary roentgen therapy.

DR. STEVENS (closing). A number of years ago Dr. Healy read a paper in Detroit, and I think he remarked that he had never known of a single patient under the age of thirty who had lived five years with cancer of the cervix. One of my cases has gone seven years and I did not know whether that was a record or not.

DR. WILLIAM P. HEALY, New York City. In answer to Dr. Stevens, we have recently reviewed four groups of five-year cases, 1928, 1929, 1930 and 1931, and there is not a single living one under thirty years of age. On the other hand, there are other series of five-year cases prior to that, where cases under thirty years of age have lived, and we have some living nine or ten years but they are relatively few.

DR. HOWES (closing). I am familiar with the work of Dr. Martin on this subject and have of course included his work in our bibliography. I do want to emphasize the frequency of this complication and its death-dealing character. Also, I would like to add that we realize the dangers of over-irradiation to the ureters and because of this danger we have not used interstitial radium either in the cervix or parametric structures, except in the case of treatment of the cervical stump following hysterectomy. However, we feel that at present we cannot reduce our total dosage to the pelvis because of possible danger of an irradiation fibrosis.

DR. BOWING (closing). Our preliminary or early observation of the results of treatment of non-neisserian pelvic inflammatory disease by means of sulfanilimide, as encountered in the course of radium treatment of carcinoma of the uterine cervix, is decidedly encouraging. The prompt and lasting response to the drug has permitted us to continue radium treatment and in one case, to complete radium treatment. Judicial administration of the drug demands clinical experience. Therefore, the patient should be treated by an attending physician in order that the effects of the drug may be followed and serious toxic effects eliminated.

I am much interested in the case of fracture of the neck of the femur reported by Dr. Johnston. I do not know of a similar case in our files. We have encountered metastasis to bone in cases of carcinoma of the cervix. However, the latter complication, in our experience, has occurred infrequently.

Concerning the discussion of the medicated vaginal pack: The foul odor associated with prolonged vaginal packing is difficult to control. The preparation of glucose mentioned is of interest to me since we have employed the method of Dr. Nicholas Senn in applying powdered sugar to necrotic malignant wounds in the groin, thoracic wall, and so forth. The

knee-chest position has greatly facilitated packing of the vagina with gauze, as well as removal of the gauze. In the management of certain types of vaginal bleeding, a small gauze sponge, moistened with concentrated acetone bactericidal solution, is applied to the surface of the bleeding area and the vagina is tightly packed with gauze. At the end of twenty-four hours, a portion of the packing is removed. A small sponge and about ½ drachm (2 gm.) of white petrolatum is placed in the vagina. The following day the remainder of the vaginal packing is removed but, should there be any tendency to bleed, further removal of gauze is abandoned and a small petrolatum sponge again is placed in the vagina. On the following day, all the packing may be removed and there is little or no tendency for the surface of the tumor to bleed. The acetone sponge on the surface of the tumor remains in place until it separates without causing bleeding. This technique has proved effective, especially in control of the oozing type of vaginal bleeding. Occasionally a more serious type of vaginal bleeding is encountered. Then packing alone is not sufficient: compression also is necessary. In this event, iodoform gauze is used as packing material. The vaginal cavity is tightly packed and the packing is continued through the vaginal outlet. The labia are separated and a suitable amount of gauze is placed against the packing; this acts as a compress against the stem of packing that protrudes from the vagina. One end of a strip of adhesive plaster is fastened to the mons veneris and the strip is brought up tightly against the perineum and fastened to the lumbosacral region. A catheter has been previously introduced. As a rule the vaginal pack remains dry and free of odor.

The inquiry concerning the time of roentgen treatment in cases of carcinoma of the uterine cervix at the Mayo Clinic may be answered as follows: Briefly, the radium is applied first and this is supplemented by a course of roentgen therapy. The total time for the combined treatment is about four weeks for the average lesion of Stage III. Following an interval of three months the patient is reexamined or reconsidered. As a rule, the primary lesion has healed well and, in all likelihood, a second course of roentgen therapy will be given.

I am greatly interested in the newer method, in which roentgen therapy is applied first and this is followed by radium therapy. The time required is much greater than for our present technique and this may be of economic importance. For example, Dr. Healy's technique requires twenty days or more for the roentgen therapy and then a rest period of twenty-eight days, at the end of which time radium is applied. In all probability, a total of sixty days is required as compared with the time necessary to employ our present technique, in accordance with which radium is followed by roentgen therapy in a period of twenty-eight days. In the past, I have observed cases in which roentgen therapy preceded radium therapy. I fully realize the cases were few and the techniques varied greatly, so my impressions may be faulty. However, all things considered, I feel reasonably certain that a greater response of the primary lesion would have occurred if radium had been applied instead of roentgen therapy. Radium therapy as the initial treatment seems most logical in that it is the most direct and effective attack possible for the primary lesion. And further, when properly applied, and if intervals are suitably timed, the customary response is satisfactory. I fully appreciate and value greatly Dr. Healy's opinion, and I hope the technique he advocates will prove to be a superior one in that the initial and late result will be greatly superior to that now reported.

Dr Pomeroy (closing). If it is not out of order I should like to ask one question. Were the patients with fractured femoral necks irradiated over the lateral pelvis fields? (The majority were not.)

I have another vaginal antiseptic to suggest, namely, acriflavine. When this first came out I thought it was only another fancy colored dye, but I now know that it can keep the vaginal packing clean for as long as four or five days. We have not seen any proctitis due to the barium enemas.

Another question I should like to ask Dr. Ullmann is in connection with cases of cardiac failure. He says there were no cases of metastasis to the heart. I should like to call your attention to an unpublished series of cases from the City Hospital of Cleveland. In a series of 10,000 autopsies there were approximately 1,000 cases of cancer, and of these 100 showed involvement of the heart or pericardium by metastatic cancer. In cases of cancer in general there is, according to these figures, a 10 per cent chance of metastatic involvement of the heart or pericardium.

# THE TREATMENT OF INJURIES PRODUCED BY ROENTGEN RAYS AND RADIO-ACTIVE SUBSTANCES*

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SEVERE injuries of the skin following the use of roentgen rays and radioactive substances have fortunately become much less frequent in the past several years; increasing knowledge of the biological effects of roentgen rays, technical improvements in the construction of apparatus and the protection against radiation, and better training of physicians and personnel have reduced considerably the occurrence of the undesirable after-effects which were formerly so frequent. The fact that burns of the skin produced by roentgen rays or radium are still occasionally encountered is due to the peculiar behavior of the rays characterized by late development of injuries of the skin, making their use by individuals without adequate training so dangerous. The reason for this late manifestation of radiation injuries is not completely cleared up; however, it is probable that it may be mainly attributed to changes in the vessels of the irradiated tissue. Rost in 1915 suggested that the effect of roentgen rays is exerted particularly on cells which have a special power of proliferation, such as the adventitial cells of the smaller vessels. These cells are of special importance in the repair of tissue and have therefore been designated by Rost as "tissue builders" (Gewebsbaumeister). Extensive injury of such cells results in the loss of reparative power of the affected tissue. Consequently, when such tissue injury has occurred there is no possibility of spontaneous healing. Purely symptomatic treatment of such tissue injuries, therefore, offers no favorable prospect for healing, for the necessary active regenerative elements are not present. The therapeutic results of the past three decades have shown that the methods of treating such radiation injuries have been rather unsuccessful.

There is scarcely a method of treatment that has not been tried for radiation injuries of the skin; for obvious reasons, such methods have been principally of the type employed for the treatment of ordinary burns. But these methods, except for an occasional favorable result, have not been effective and these patients who have gone from one physician to another with apparently incurable burns have painted a sad picture of the medical profession's helplessness in this condition. In addition to lawsuits for the physician, and the danger of morphine addiction to which these patients all invariably succumb because of the severity of their pain, these cases are unpleasant for they are the result of physicians' work, even though the injury may have been unintentional and often without blame. And if such injuries occur in patients who received radiation therapy for lesions of minor or purely cosmetic importance, there is all the more reason for seeking an effective method of treatment.

Since, as has been mentioned, symptomatic treatment is ineffective, and surgical and plastic procedures cannot always be employed, it is not surprising that in the search for a specific cure many methods of treatment have been attempted. In this connection one may mention periarterial sympathectomy, according to Lériche, variation of the acid-base equilibrium, recommended by Kalk on the basis of personal observation of one case favorably affected thereby, and the dietary treatment of Gerson - Sauerbruch - Hermannsdorfer, which has been recommended by Bommer.

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† Now at the Tumor Clinic, Michael Reese Hospital, Chicago, Illinois.

Extensive trial of the above described methods has shown that good results were the exception and could be obtained only in occasional cases and were not to be expected in the majority of similar cases. Therefore, such methods of treatment have been discarded. The one method of treatment for radiation injuries that has gained popularity, and concerning which Bordier and Milian have written in the French literature and Holfelder in the German, is the treatment with the cold cautery. Until the development of the method to be described, I used the cold cautery exclusively in the treatment of radiation injuries and am of the opinion that it is not of great value as a general method of treatment. For the milder degrees of skin change, such as telangiectasia, pigmentation and skin atrophy, the method has no practical value; similarly the scleroderma-like keratoses cannot be affected by this method, so that its use remains limited to ulceration. When these ulcerations show elevated borders or when papillomatous proliferations develop at the base of the ulcer, the cold cautery may be used; for other cases, this method of treatment is not applicable. In general, the extent of the ulcer does not correspond to the limits of injured skin; it is localized to the harder parts which are more or less affected by the irradiation and lack reparative power as a result of this irradiation. It is often to be observed that the skin defects following operation with a cold cautery heal slowly and incompletely, for the spontaneous tendency to healing is diminished in areas damaged by irradiation. The result is that not infrequently the cautery adds a second lesion. This combination is then best treated by extensive surgical plastic procedures, which, however, the patient is inclined to consider the undesirable sequela of an error in the original therapy.

The unsatisfactory results in the treatment of radiation injuries of the skin persuaded me some ten years ago to look for a method which would yield better therapeutic results and yet have the advantages of simplicity and painlessness. After two years of preliminary experimental work I was able to report in 1930, for the first time, a series of roentgen burns in which it was possible to produce complete healing in a relatively short space of time *by the use of radium emanation* (*radon*). The first objection to this method of treatment, expressed at the time and occasionally still mentioned today, is that one is adding further radiation to a tissue already injured by previous irradiation. This objection is unimportant since the injuries are produced by the roentgen rays and by the gamma rays of radium whereas, in the therapy with radium emanation, according to my technique, alpha rays are used predominantly. That this factor is most important and that the treatment is without danger to the patients in all cases is illustrated by the results of treatment obtained by myself and other colleagues in the past eight years. The best proof of the importance of the qualitative composition of the rays for the curing of the lesion is the result of treatment in a patient in whom it was possible by the use of alpha rays to cure an injury of the skin produced by beta rays of radium.

I have personally treated a total of some 70 patients having very extensive and severe roentgen burns who, with few exceptions, had been treated without success for many years by other physicians. Many of the patients had become morphine addicts, in others amputations of portions of limbs or of entire limbs had become necessary. Others had either refused treatment or had been treated unsuccessfully by charlatans and quacks. In all of these patients extensive and, above all, good cosmetic improvement took place; in the large majority of cases there was complete healing and relief of the suffering of many years' duration; in all cases in which there was not a prompt response to the therapy, infractions in technique or dosage could be demonstrated following the correction of which cure took place. In the treatment of over 70 patients I have seen only 2 who

FIG. 1. *A*, burn of five months' duration; *B*, result after three weeks of radon treatment.

were not completely cured and will discuss these critically later. The large number of complete cures (in no disease can one hope to attain 100 per cent curability with the same therapeutic agent) justify the use of the procedure, especially since there is no difficulty, no inconvenience or expense associated with its use.

In my previous work, I have pointed out that the crux of the problem of radon therapy depends on dosage and to avoid repetition will at this point describe briefly the technique of application and the requisite doses of radium emanation.

Radium emanation (radon) in the form of an ointment is used exclusively in this treatment. Strasburger has pointed out that vaseline will absorb nine times as much radium emanation as a similar volume of air and thirty-six times as much as water at room temperature. We have made use of this favorable physical combination and employ white or yellow vaseline as a solvent for the radium emanation. The concentration amounts to 50 to 100 electrostatic units per gram of vaseline. It is ordinarily inadvisable to exceed 100 e.s.u.; on the other hand, a satisfactory result is usually not obtained with less than 50 e.s.u. per gram; more specific directions for dosage cannot be given for they depend upon the individual case, the dose being increased or diminished depending upon the condition of the skin at the time and being judged only on the basis of personal experience.

Since this radon ointment has a half-value period of about four days, it must be prepared fresh for use or its dose calculated to contain the necessary quantity of radon on the day of use. The ointment is applied directly from a container or with the help of a spatula to the area of skin to be treated and is immediately covered with a piece of rubber dam or oil cloth or cellophane of suitable size. It is held in place by adhesive strips under which absorbent cotton has been placed. The ad-

hesive is laid down in overlapping strips to prevent the escape of emanation into the air. The dressing is left in place eight hours and is then removed by the patient. The treatments are repeated at intervals of seven days so that subsequent treatments are always administered on the same day of the week. In the interval between treatments the skin must not be irritated by any medication and is best covered by a 10 per cent boric-beryllium ointment.

All cases of skin injured by roentgen rays and by beta and gamma rays of radium, especially late injuries with deep ulcerations, are suitable for treatment with radium emanation. Favorable results may also be anticipated in cases of skin induration and scleroderma-like keratosis, as well as in the lesser degrees of skin injury, such as telangiectasia. The severe pain which produces morphine addiction in many patients is relieved in most cases after the first application; and I have seen a large number of patients whose addiction to narcotics was rapidly cured thereby. The number of radon treatments depends on the depth and the extent of the process; for the smaller ulcerations three to four applications are necessary; for the extensive burns with associated bone necrosis more treatment may be necessary. It is important to remember that overdosage may lead to failure as well as underdosage; that the interval between treatments must be observed, and that all additional and irritating therapy must be stopped.

As already mentioned, in the past eight years I have treated 70 very severe roentgen burns by this method and have been consulted by colleagues, personally or by letter, in an equally large number of cases. Among these cases, there are numerous radiologists and roentgen technicians who were relieved and cured of their suffering

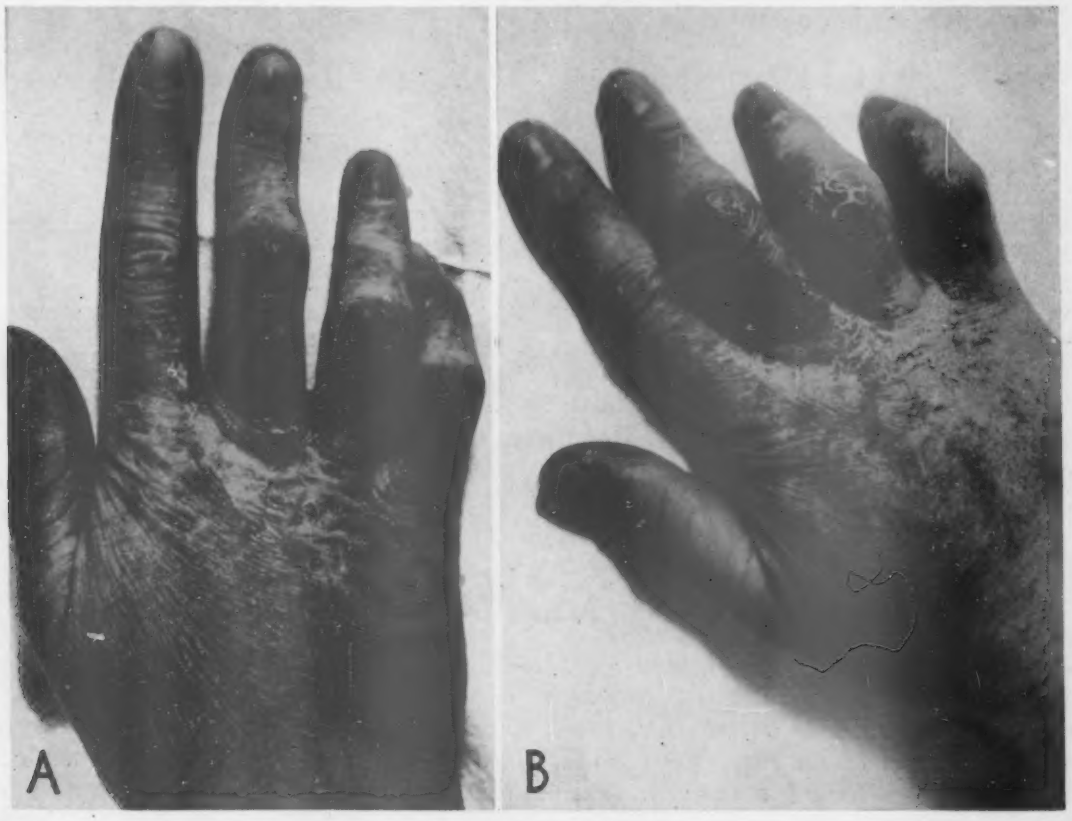


Fig. 2. *A*, roentgen burn of fourteen years' duration; *B*, result after one single treatment with radon.

FIG. 3. *A*, roentgen burn of thirteen years' duration following radiation treatment for suspected cancer of the esophagus; *B*, same case after five weeks of treatment with radon.

for the first time. I cannot give a detailed report of each case here and will limit myself to several illustrations which show clearly the results of treatment. With one exception, these are cases in whom the burns had been in existence at least five years, during which time the patients had been under observation and treatment by physicians, without improvement. Many of these patients had been suffering from their burns for more than ten years, 5 longer than fifteen years and 1 patient over twenty years; several had given up after ten to twelve years of fruitless therapy and had become morphine addicts. In other patients, extensive plastic operations had been performed which later underwent necrosis; in others, the condition had already progressed to carcinoma.

Figure 1 shows a woman who had received intensive roentgen therapy for carcinoma of the breast and as a result of overlapping of the fields developed a roentgen ulceration shortly after completion of treatment, which did not heal despite months of therapy. The clinical picture was the usual one: indurated skin with telangiectasis, in the center of which was a large ulcer the size of a child's hand. After three applications of radium emanation the ulcer epithelialized completely and has remained healed; the surrounding skin became softer, the telangiectases regressed.

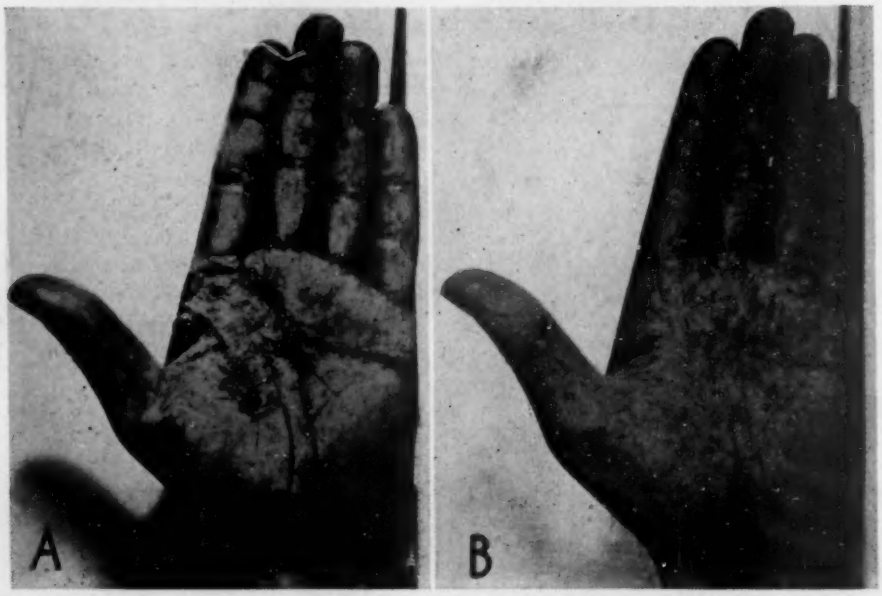


FIG. 4. *A*, roentgen burn of twelve years' duration; *B*, same case after six weeks of radon treatment.

Figure 2 is a patient with a radiation injury of the right hand of fourteen years' duration. For nine years this patient had been under the constant treatment of a physician during which time the ulceration and contracture had developed. Among other things thorium X had been used without result. The photograph

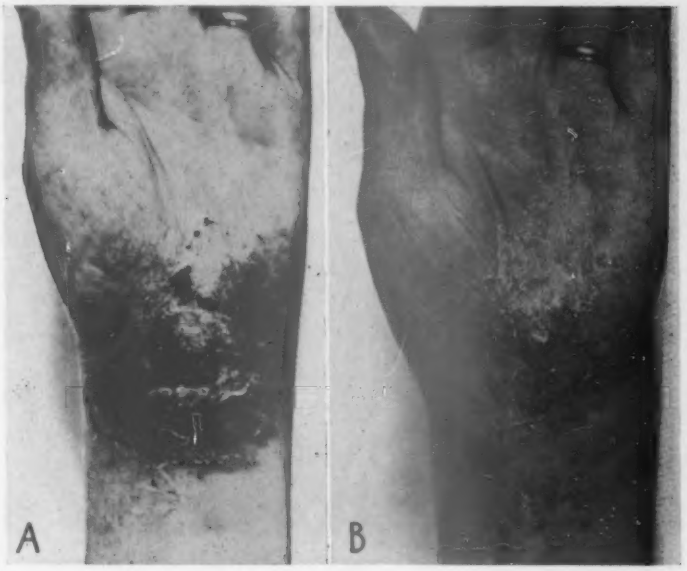


Fig. 5. *A*, lesion following roentgen irradiation for tuberculosis of the wrist; *B*, same case after eleven weeks of treatment with radon.

shows the condition after a *single* application of radon, with three of the smaller ulcerations already healed and the largest ulcer considerably diminished in size. After a total of five applications all the ulcerations had healed, the skin was softer and flexible, the telangiectasis had regressed, the mobility of the fingers had improved and the severe pains had disappeared.

Figure 3 shows a patient who had received intensive roentgen treatment for a suspected carcinoma of the esophagus. For thirteen years the right side of the neck had presented first extensive induration of the skin and telangiectasia and then the development of an ulcer which had not healed despite prolonged treatment. After three applications of radium emanation the ulcer had disappeared and after five treatments the telangiectases were gone.

Figure 4 shows the left hand of a patient treated with roentgen rays for eczema. Extensive induration of the palmar surface of the hand with telangiectasis had been in existence for twelve years. At all the joints there were small ulcerations of the skin which had not improved despite prolonged treatment and had impaired the mobility of the joints considerably. After six treatments with radon the ulcerations had healed, the induration had softened,

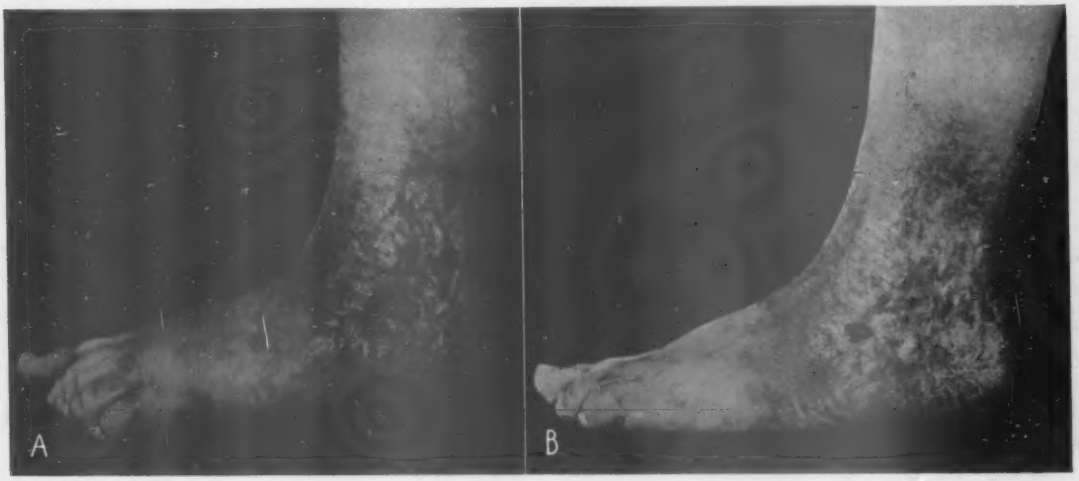


Fig. 6. *A*, roentgen burn of eleven years' duration; *B*, same case after ten weeks of treatment with radon.

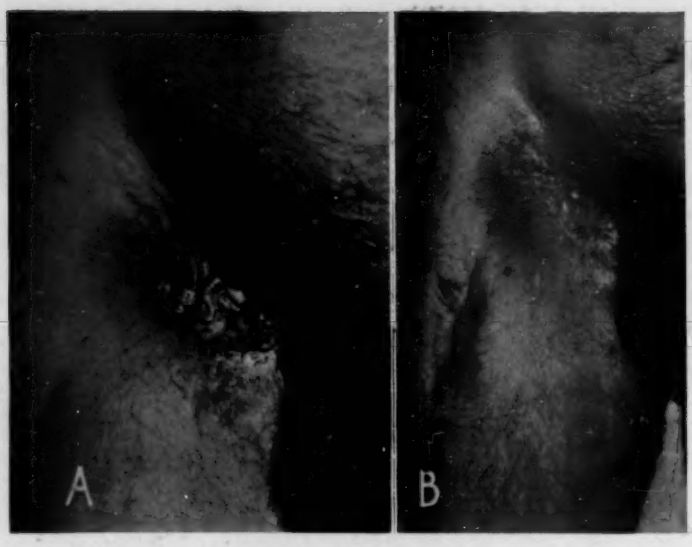


FIG. 7. *A*, Lesion of sixteen years' duration following roentgen irradiation for tuberculosis of the right groin; *B*, same case fourteen weeks after treatment with radon.

the atrophic fibrotic bands had disappeared and the telangiectases had regressed.

Figure 5 shows a patient treated with roentgen rays for tuberculosis of the wrist. The injury to the skin had been in existence for fourteen years and had been treated without success during this entire period of time. The ulceration was deep and painful; there were marked induration and telangiectasis. After eleven treatments with radium emanation the injured area showed, as can be seen in the photograph, ulceration completely healed, skin soft, wrist joint freely movable, most of the telangiectasis gone, pain completely disappeared.

Figure 6 shows a roentgen burn of the left foot of a patient irradiated for tuberculosis. The ulceration, induration and telangiectasis had been in existence for eleven years with no improvement despite prolonged hospitalization during this time. The attending physicians had recommended amputation to enable the patient to carry on her work and she was prepared to undergo this operation. After ten treatments with radon the ulceration had healed, the induration had softened, the mobility of the limb had improved and only a slight amount of telangiectasis remained.

Figure 7 shows a patient treated with roentgen rays for tuberculosis of the right groin. Ulcers had been in existence for sixteen years and caused such intense pain that the patient had been obliged to give up his work as a waiter. He had been treated for many years unsuccessfully. After fourteen treatments with radium emanation not only had the ulcer healed but the previously board-like induration of the surrounding skin had regressed so far that the patient could resume his occupation.

Figure 8 shows a roentgen burn on the extensor surface of the left forearm of a physician who had received excessive dosage of roentgen

FIG. 8. *A*, roentgen burn of twelve years' duration with cancer formation; *B*, same case nineteen weeks after treatment with radon.

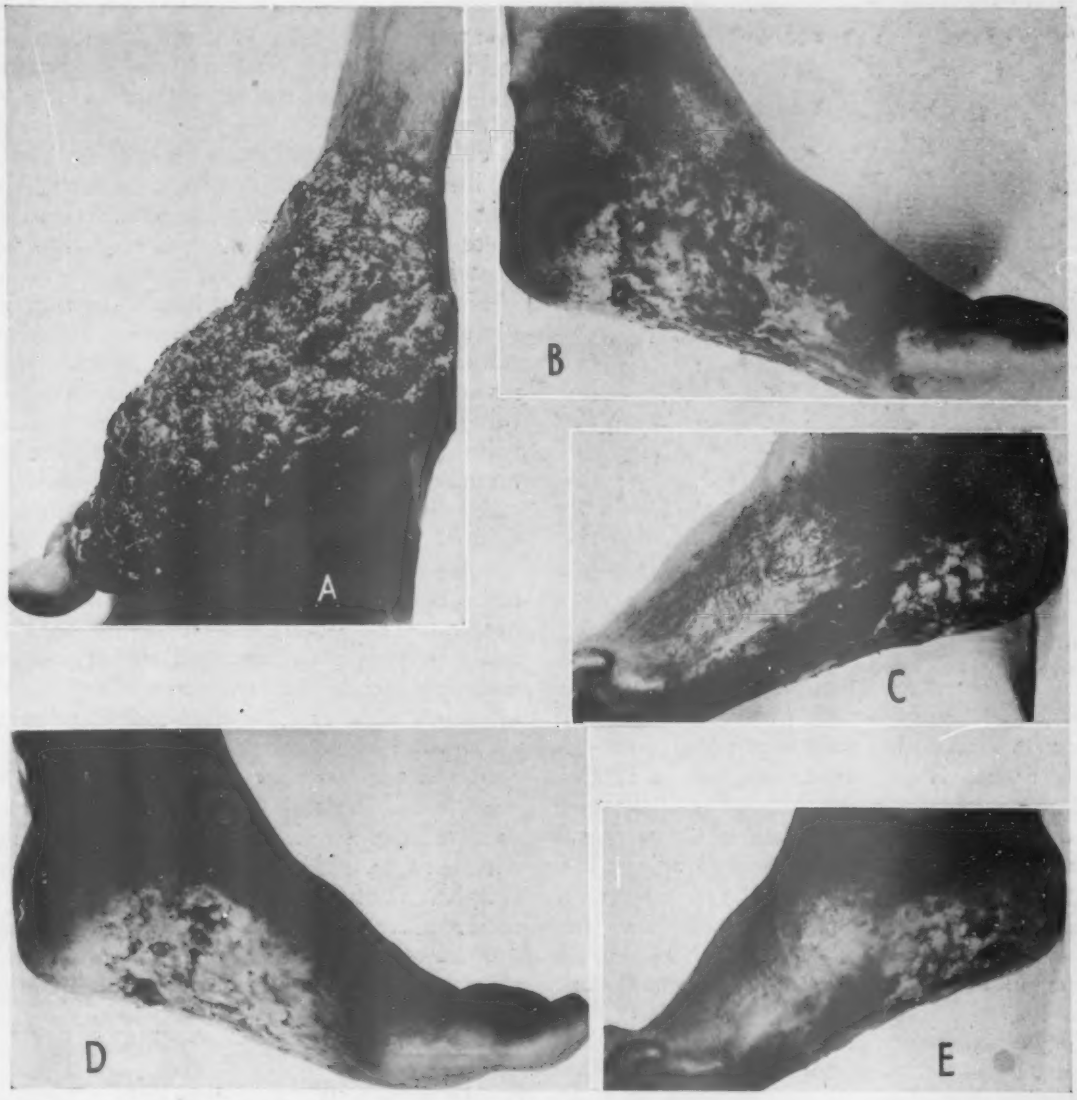


Fig. 9. *A*, roentgen burn of right foot of sixteen years' duration, with development of cancer; *B* and *C*, left foot after removal of part of lesion with the cold cautery before radon treatment; *D* and *E*, same case seven weeks later.

rays for psoriasis. The upper half of the forearm showed a large moist ulcer with sluggish granulations and extensive induration of the surrounding skin, and the pain was so intense that this physician had to give up his practice. He had suffered for twelve years and was treated unsuccessfully during the entire time. Following nineteen treatments with radon the condition was so improved that only a superficial erosion remained in the center of the original ulcer and the pain had disappeared completely. The induration of the skin and the telangiectasis had regressed considerably.

The next group of illustrations (Fig. 9) shows a patient with roentgen burns of both feet, of sixteen years' duration. In the right foot ulceration had extended to the bones and a carcinoma twice the size of a fist had developed, necessitating amputation of the right leg. The patient had refused to undergo amputation of the left foot so that the malignant tumor of this extremity was destroyed with the cold cautery. The condition, however, was so serious that in spite of prosthesis and crutches the patient could scarcely move. The patient had been treated for years and during the preceding six

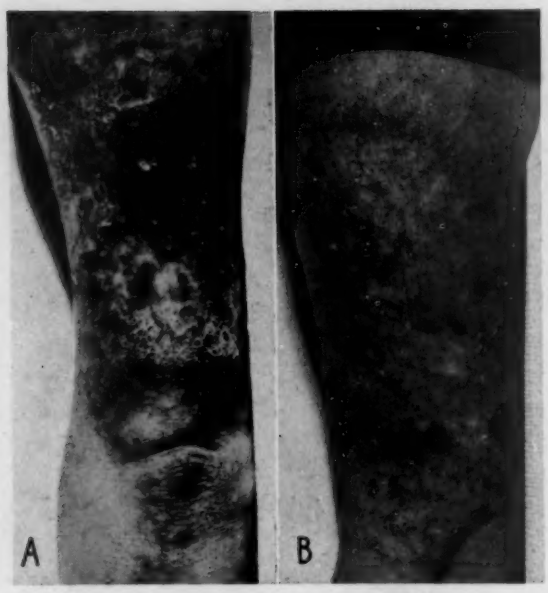


FIG. 10. *A*, roentgen burn after treatment for lupus of arm—twenty years' duration; *B*, same case eight weeks after radon treatment.

years had been exposed to several thousand applications of Finsen light. After seven treatments with radium emanation there was considerable improvement. The pains had gone and the induration had softened; all the small ulcers on the sole of the foot had healed and only a remnant of the two larger ulcers remained; on the medial and lateral borders, the ulcers had so flattened out that there was no bone exposed anywhere. There was further improvement following continuation of treatment.

Figure 10 shows a patient who had received frequent roentgen treatments for lupus of the left arm. This very deep roentgen burn was of twenty years' duration and was characterized by intense pain and extensive induration. After eight treatments with radium emanation complete healing took place, so that only a thin atrophic skin remained at the site of the injury.

Figure 11 shows a patient with a roentgen ulcer of the right side of the neck of ten years' duration. The condition was complicated by a severe diabetes. After many years of unsuccessful treatment, it was hoped that a curative result might be obtained with insulin. After three months of hospitalization it was possible to reduce the blood sugar to 140 per cent and the urine became sugar- and acetone-free; the ulcer became quite clean during this time but showed no tendency to healing. The patient left the hospital, did not adhere to diet so that the blood sugar rose to 212 mg. per cent and acetone appeared in the urine. In spite of this the ulcer healed after eight applications of radon and has remained completely healed.

Figure 12 shows a patient treated with radium for psoriasis who developed a severe burn as a result of a technical error and overdosage with beta rays; this injury involved the terminal phalanx of the thumb, had extended to the bone and resulted in a bone necrosis. The pain was unbearable. In the absence of any tendency to heal during a period of three months and be-

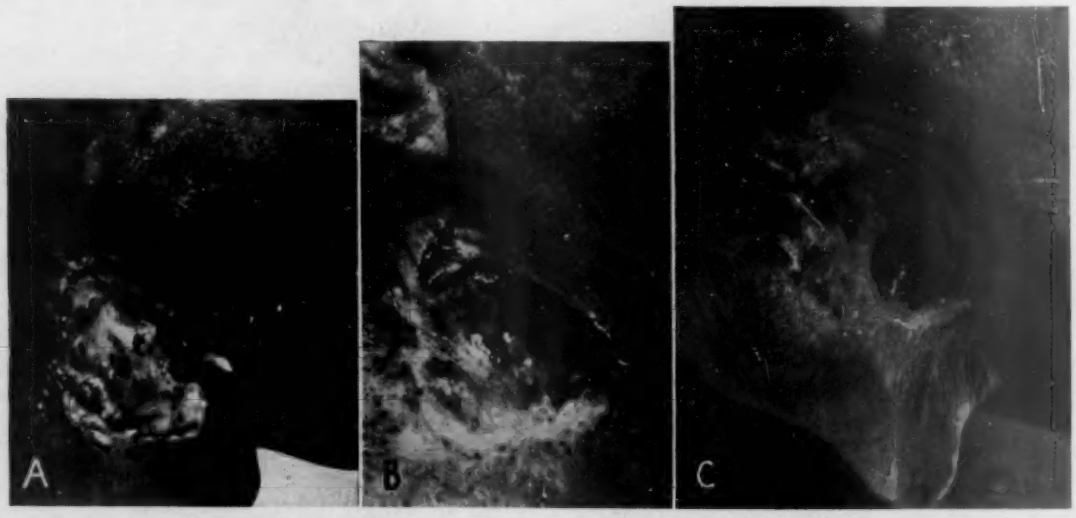


FIG. 11. *A*, roentgen burn of right side of neck of ten years' duration complicated by severe diabetes; *B*, same case four weeks after radon treatment; *C*, same case eight weeks after radon treatment.

cause of the loss of motion of the thumb, the question of amputation arose as a last resort. At my recommendation it was decided to try radium emanation and the result of this treatment which was carried out in seventeen applications is obvious from the illustration. The pain disappeared after several treatments, the mobility of the thumb returned and the terminal phalanx could be preserved.

The last illustration (Fig. 13) is one which, strictly speaking, does not belong to this subject, but it is shown as an example of the possibility of producing healing in wounds, by the use of radium emanation, which have proved refractory to other methods of treatment. This case is a varicose ulcer of the leg of a man, aged twenty-one, which had been in existence for four years despite considerable therapy. Ointments, compresses, diathermy, massage, roentgen therapy, sodium chloride injection into the veins and antiluetic therapy had all been attempted unsuccessfully. After twelve treatments with radium emanation the ulcer healed. Two months later a pea-sized recurrence appeared which healed quickly after further radon treatments and has remained healed.

Fig. 13. *A*, varicose ulcer of four years' duration; *B*, same case after twelve weeks of treatment with radon.

Several observations may be made to supplement these illustrations. Not all of the patients were photographed following a favorable result from treatment; in many cases the photographs were made during the course of treatment while the patients were receiving radon therapy. I have not been able to follow all of these patients to complete and final healing, and one knows how difficult it is to persuade patients to return for examination when there is no further need for treatment. Since the larger proportion of the patients treated by me live in Germany and in Scandinavia it is to be understood how difficult and often impossible it was for me to obtain photographs while in Istanbul. Likewise, in some of the patients, treatment was not continued in the manner I prescribed. But despite all these limitations I believe that these illustrations will give some impression of the favorable results which can be accomplished for the otherwise refractory radiation injuries of the skin.

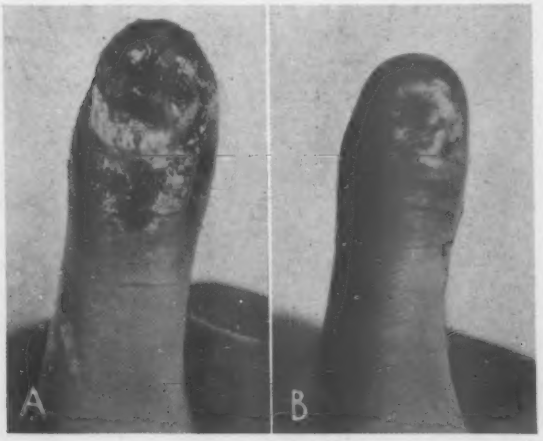


Fig. 12. *A*, radium burn produced by beta rays—three months' duration; *B*, same case seventeen weeks after radon treatment.

Finally, a word about the few cases in which radon emanation did not produce the expected result. I mentioned 2 cases of the 70 in which complete healing could not be obtained. These 2 cases in which considerable improvement resulted, but not complete clinical cure, are the ones with the extensive involvement of the foot and the doctor with the burn of the fore-

arm. In these cases with incomplete healing there was carcinoma at the base of the burns in addition to the roentgen injury, and these carcinomas were naturally not cured by the small doses of radon used therapeutically. As a further explanation, I submit the following brief description of a case which I have observed:

A girl who had been treated with roentgen rays for hypertrichosis developed extensive induration of the skin with telangiectasis and finally ulceration of the left cheek. This burn was of eighteen years' duration. After four treatments with radon the ulceration (4 cm. in diameter) healed and the patient did not return. One year later she came back with an ulceration 3 cm. in diameter just below the previous ulcer. With further radon therapy the ulceration decreased to the size of a pea after two treatments. It remained this size, however, and did not respond to further treatment. A biopsy of the border was performed and the section showed squamous cell carcinoma. A wide elliptical excision was performed (this being easily accomplished after the preceding radon therapy), followed by a plastic repair of the defect, and healing resulted.

I have observed a similar case of a large burn in the gluteal region (20×30 cm.) following roentgen treatent for carcinoma of the rectum. Radon therapy diminished the size of the ulcer considerably but a small defect remained. The biopsy confirmed the diagnosis of carcinoma.

From these observations I have concluded that all cases in which properly executed radon therapy does not lead to complete healing of the ulceration or which appear to be refractory after a certain interval must be suspected of having undergone carcinomatous change, even if clinically the lesion does not appear carcinomatous.

To summarize briefly: I believe that the illustrations speak more clearly than any verbal explanation, and I am of the opinion that in radium emanation properly applied in correct doses we have at our disposal an effective method of treating radiation injuries, a method whose effectiveness has been demonstrated in a large number of patients. I can only tell of my personal experiences and invite a verification of my results. There is only one criterion of a therapeutic method—its results.

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# THE INHERITANCE STRUCTURE OF THE CELL AND ITS RELATION TO IRRADIATION EFFECTS*

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IN THE life sciences radiant energy is of interest to three distinct groups of investigators. Those using roentgen rays for diagnostic purposes would prefer that the absorbed rays had little permanent effect on the tissues exposed to them. Those using roentgen rays in treating growths desire the immobilization of the abnormal tissue without the surrounding normal tissue being affected. The third group of workers focus their attention on the cells which, although absorbing enough energy to produce observable effects, have not enough to cause their complete destruction. The question significant to all three groups in attaining their objectives is the old one—what changes are wrought by the absorption of radiant energy in the cell?

This question has a partial answer in the researches in cytology and genetics. Hertwig[8,9] observed that irradiated chromosomes were frequently abnormal. Later genetic research with the extensive mapping of the chromosome structure with genes showed the extent of these abnormalities. The hereditary units of the cells, the genes, are mutated to others having new properties. A discussion of how completely these effects will account for the observed changes following roentgen treatment is the subject of this paper.

The survival curves for a number of organisms under different roentgen exposures are available, thanks to the work of several different investigators. The species for which data are at hand include the typhoid bacteria,[20] Algae,[10] yeast,[21] *Drosophila* eggs,[11–18] and sperm,[6] *Ascaris* eggs,[1] salamander eggs,[10] bean, sunflower and mustard seedlings,[4] protozoa,[2] etc.[5] Much of this material, despite its excellence from the roentgen-ray standpoint, is not suitable for our purposes. Some lack studies on the cytology of the cells or tissues which are irradiated. Others are lacking in a knowledge of the genetic behavior of the organism which is exposed to roentgen rays.

In this discussion I propose to examine some old and some new data bearing on this problem of the interdependence of the inheritance structure and irradiation effects. For this purpose the object of irradiation must necessarily have had extensive study from many viewpoints. Single-celled entities or even a part of the cell gives most information since the effects on individual elements need to be separable. Such material is limited and has the danger of being only a special case. Yet without such material the irradiation effects defy analysis.

One of the most frequently observed effects of irradiation of tissue, and indeed the objective of one of the groups mentioned earlier, is the destruction or inactivation of the cell irradiated. This inactivation may be attributed to primary effects on the chromosomes and their contained genes, to changes in the cytoplasm or to both jointly. Our problem calls for differentiating these effects and assigning to each element its respective rôle in the observed death rates. The data on the effect on survival rates of *Drosophila* eggs, *Drosophila* sperm, the sex chromosome of *Drosophila* and the individual genes when exposed to different amounts of radiation are worth discussing from this viewpoint. The survival curves for these materials are shown in Figure 1. The curve for the *Drosophila* eggs is taken from Packard's noteworthy researches.[11–18] These eggs are diploid. Precautions were taken to have them over one hour and less than three hours from the time they were laid to the time they were irradiated. Development of

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the *Drosophila* egg in its early stages comes through division of the nuclei without formation of cell walls. The time necessary for a nuclear division is ten to twenty minutes. If each division cycle proceeds at this rate the eggs should have an average number of $2^6$ to $2^{12}$ nuclei when they are irradiated.

gene dimensions which is capable of separation from the cell, allowing purification and controlled roentgen exposure.

Figure 1 shows the relation which ionization dosage of roentgen rays has to the rate of inactivation of the *Drosophila* eggs, sperm cells or virus particles. The largest

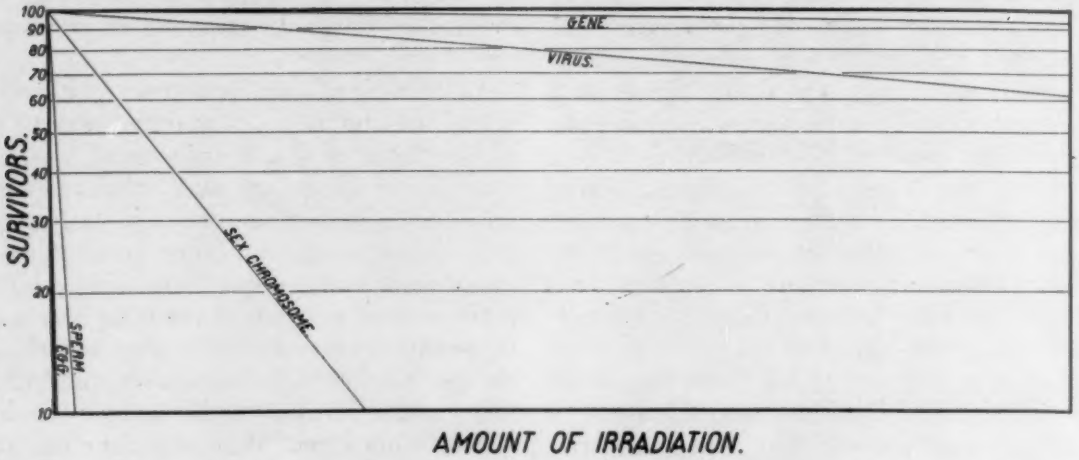


FIG. 1. Inactivation rates of *Drosophila* eggs, sperm, sex chromosomes, genes and tobacco mosaic virus when exposed to measured amount of roentgen-ray energy.

The irradiated *Drosophila* sperms were obtained by treating wild type males thirty hours after hatching. Sperms having but a single complement of chromosomes are haploid. The effect of the treatment on a portion of the sperm, the sex chromosome, may be separated from that of the whole sperm. Changes in genes causing visible but not lethal effects may be separated from those causing death. Curves showing these separate effects are inserted in the chart.

Besides the effects on *Drosophila* eggs and sperm, we also include data on the influence of irradiation on the virus of tobacco mosaic taken from the work of Dr. Price and myself.[7,19] This virus is composed of particles the size of which is estimated to be of the same order as that of genes. Like genes it is incapable of reproduction outside of living cells; it produces similar effects on its host tissues, as for instance, variegation or mottling; it mutates to new forms which retain the ability to reproduce themselves. This virus offers a particle of

entities are the egg cells. They are inactivated more rapidly than the sperm cells. The sperm cells are larger than the sex chromosomes and are inactivated at a greater rate. The inactivation of these cells proceeds at a much faster rate than the virus, tobacco mosaic. The size of the sex chromosome is less than that of the sperm but much greater than that of a virus particle. The sex chromosomes are inactivated at an intermediate rate. Genes are of the same order of size as or smaller than tobacco mosaic virus particles. The data show that the genes are changed by roentgen irradiation at a lower rate than any of the other substances listed. Evidently the size of the element exposed to the roentgen rays bears a direct relation to the effects produced.

An intelligent appreciation of the size of these different materials is favored if they are listed in terms of some commonly used unit. For this purpose we shall use the centimeter rather than the millimeter or micron. As the objects are small in size

they may for convenience be kept in multiples of 10, i.e., $1\times10^{-6}$ cm. equals one millionth of a centimeter. *Drosophila* egg cells are about $5.0\times10^{-2}$ cm. in length and $2.0\times10^{-2}$ cm. in breadth and thickness. If considered a rectangular block, the volume is $2.0\times10^{-5}$ cm$^3$. The volume of a *Drosophila* sperm head is $7.4\times10^{-13}$ cm$^3$. The size of the virus of tobacco mosaic particle is, according to the result obtained by the ultracentrifuge, $4.3\times10^{-17}$ cm$^3$. Estimates of the size of the gene have a fairly large range, that of the writer being smallest, $1\times10^{-18}$ cm.$^3$

We may convert the volumes of these different materials into the proportion which their size bears to that of the *Drosophila* egg. These ratios from largest to smallest are: first, the egg to itself, sperm, sex chromosome, virus particle and gene, the quantitative relations being as follows:

$$1.0:4.0\times10^{-5}:8.0\times10^{-9}:2.1\times10^{-12}:5.0\times10^{-14}. \quad (1)$$

The different materials are inactivated when exposed to roentgen rays at the following rates per an electrostatic unit. For the *Drosophila* egg the rate of inactivation is $-5.39\times10^{-3}$ per e.s.u.; for the sperm cells the rate is $-2.31\times10^{-4}$; for the sex chromosome the rate is $-1.5\times10^{-5}$; for the virus particle the rate is $-1.0\times10^{-6}$ and for the gene the rate is $-1.0\times10^{-7}$. These rates are in the proportion of:

$$1.0:4.1\times10^{-2}:2.6\times10^{-3}:1.7\times10^{-4}:1.7\times10^{-5}. \quad (2)$$

Evidently the effect of the roentgen rays, while in the direction of a decrease in relative size being accompanied by a decrease in the relative rate of inactivation of the treated material, is quantitatively in poor accord with these changes. It would seem that some portion of the egg rather than the whole is affected by the rays.

The cell chromatin is structurally altered by roentgen irradiation. The egg at the stage when it is irradiated contains possibly $2^8$ nuclei or since the nuclei are diploid, 512 times as much chromatin as the sperm. It seems probable that this chromatin, or perhaps more properly its contained genes, is the cell structure first affected by the roentgen rays. The proportion of the chromatin in the egg cell as contrasted with that of the sperm or sex chromosome is:

$$1.0:2.0\times10^{-3}:4.5\times10^{-4}. \quad (3)$$

This proportion, while not in full agreement with the proportion which exists between the inactivation rates of the eggs, sperms and sex chromosomes (2) is in better agreement than the proportion (1) based on the gross size of the eggs. The discrepancy lies in the fact that the eggs have too slow a rate of inactivation. Consideration of other facts furnishes a partial explanation of this difficulty.

The curve for inactivation of the eggs indicates that two to four separate units of energy must be absorbed before the egg is inactivated. The curve for the sperm cells, on the other hand, indicates that the absorption of but one unit of energy is sufficient to cause inactivation. The necessity for this multiple absorption would definitely lower the rate of inactivation of the eggs as contrasted with that of the sperm. We should not expect the eggs to inactivate as rapidly as the sperm that require but one absorption of energy to inactivate. Taking this fact into consideration results in an even closer agreement between the energy necessary for the inactivations (2) and the relative chromatin volumes (3) of the different substances.

A different consideration brings the rates of inactivation for the sex chromosome into somewhat close agreement with the observations on the sperm cells. The sex chromosome, unlike the other chromosomes, has a rather large proportion of its substance composed of genetically inert materials. A comparison of the ratios of inactivation (2) with those of size (3) shows that the sex chromosome has a lower inactivation rate than expected from its size if we judge by the data on the sperm. This difference is expected if the genes are the cellular structures most affected by the roentgen rays.

The above comparisons indicate that the size of the object irradiated has a direct relation to the rate of inactivation. The comparison when on the basis of the quantity of chromatin in the egg is in better agreement with the rate of inactivation of the different materials than when the comparison is on gross egg size. This fact indicates that the absorbed roentgen rays may activating the virus particles.

The first chart in Figure 2 shows the rate of inactivation of virus as contained in expressed juice from the diseased plant. The curve for this inactivation is the type which would result if the absorption of one unit of energy in the virus inactivated it. The second chart is that for virus purified by crystallization and dissolved in a clear

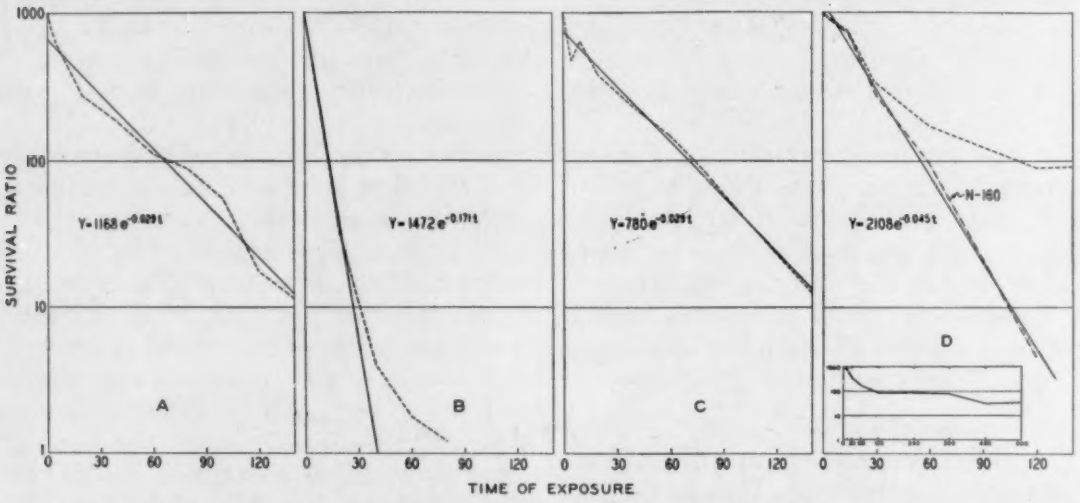


Fig. 2. Inactivation rates of tobacco mosaic virus, in different diluents and in dried form, when exposed to the same amount of ultraviolet energy.

cause most of the observed inactivation by altering the chromosomes rather than by direct changes in the cytoplasmic structures. These changes, as genetic evidence has shown, consist of changes in and elimination of genes, breaks in and rearrangement of the chromosomes.

The question arises—are these roentgen-ray changes made by direct absorption of energy within the chromosome or gene, or are they due to secondary changes brought about by chemicals produced in the surrounding medium by the energy of the roentgen rays? Up to the present the difficulty of isolating the genes from the cell has handicapped the attack on this problem.

The properties of genes are similar to those of the tobacco mosaic virus which may be isolated, purified or dried. Figure 2, taken from a paper by Price and myself,[19] shows the effect of radiant energy of the mercury quartz ultraviolet lamp in in-

buffer solution. The inactivation curve for this material is of the same type as the previous chart, the absorption of one unit of energy inactivates. The rate of inactivation is greater, however. The increased slope is interpreted as due to the removal of the ultraviolet energy by absorption in the debris contained in the expressed juice. That this reasoning is correct is shown in the third chart. A portion of the crystalline virus used in the second experiment was dissolved in the expressed juice from normal tobacco plants. The slope of this inactivation curve is the same as that of the first figure. This evidence shows that the rate of inactivation of the virus proper is essentially the same in each experiment. The chemical treatment sustained by the virus particles has in no way altered its properties, i.e., its size on exposure to the roentgen rays must have been the same, within the error of the experiment.

The fourth chart presents the inactivation curve of the virus when dried in the plant juices. The drying process fixes some of the plant debris, sometimes laying it over and shielding the virus particle from the slightly penetrating ultraviolet rays. The observed curve is no longer a straight line of constant slope. It asymptotes to the numbers of virus particles which are protected from the effects of the light. If we subtract these protected particles from the raw data to get the number of particles actually susceptible to treatment, the curve obtained is a straight line of constant slope like that for the previous charts. The slope constant is slightly greater than that observed in the previous charts. The data are subject to the same interpretation, however. One absorption of a unit quantity of energy is enough to inactivate.

The fourth chart shows that the dried virus, when capable of being reached by the ultraviolet light, is inactivated as rapidly as the virus in a water medium. From this it follows that a liquid medium is not necessary for the ultraviolet to inactivate virus. So far as the evidence goes, the direct effect of the ultraviolet light on the virus itself, rather than through some indirect chemical reaction initiated in the medium, is indicated as the mode of action of the energy.

This conclusion receives further support from the roentgen-ray experiments on virus shown in Figure 1. The virus as expressed from the diseased plant was dried on the dish before being exposed to the roentgen rays. The roentgen rays are sufficiently penetrating so that all of the virus particles are susceptible to inactivation. The curve is again of the familiar Poisson type whose derivation suggests that the absorption of but one unit of energy is sufficient to inactivate the virus.

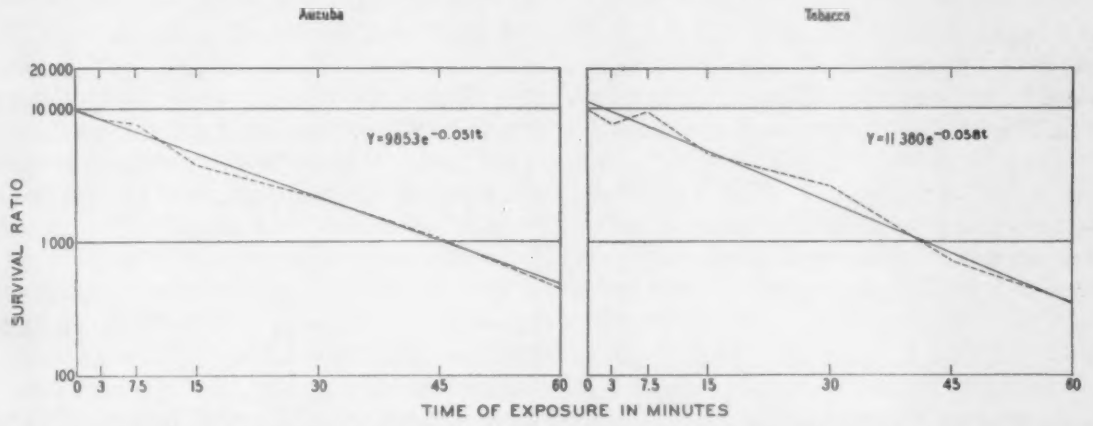


Fig. 3. Inactivation rates of tobacco mosaic virus and a mutant form derived from it when exposed to the same amounts of roentgen-ray energy.

The further problem of what roentgen rays do to the genic portion of the inheritance structure received some light from another experiment on virus. In an experiment with ultraviolet light a tobacco mosaic particle mutated to a different form, the so-called aucuba type. This changed virus was isolated in pure form. The parent virus and its mutated progeny were treated with roentgen rays to determine their inactivation rates (Fig. 3).

The inactivation rates in each case were the same. Evidence has been adduced earlier to prove that size of the object treated is a direct factor in the effect of the roentgen rays. As the roentgen dosage was the same, the results indicate that the two types of particles had the same general size within the limits of the experimental accuracy. These results indicate that in mutating to the aucuba form the virus particle underwent an internal reorganization rather than being split, on the one hand, or polymerized, on the other.

It will be noted that these two viruses, the parent and mutated form, require a large amount of energy to inactivate any significant quantity. This fact has an interest to those who may accept any hypothesis of a virus agent in abnormal growths and at the same time are attempting to treat such growths with roentgen rays. If the elimination of the growth requires the inactivation of virus of large molecular size, 20 million or less in molecular weight, then the roentgen-ray dosage to which the tissues must necessarily be exposed becomes some million of roentgens. Such an exposure of normal tissue to roentgen rays is directly against modern practice, 10,000 r per month being considered the safe maximum. As it is possible to reduce certain tumors, if taken when they are small enough, by treating them with doses of 1,000 to 3,000 r, it follows that for these growths a different mechanism of control from that of the inactivation of a virus must be postulated.

Experimental verification of this conclusion is found in preliminary experiments of Price and myself. A tobacco leaf infected with tobacco mosaic virus may have the virus destroyed if the infected leaf is exposed to radiant energy over a sufficiently long period. This period is of the same length as that necessary to destroy the virus if it is just extracted from the leaf and the juice exposed to the radiant energy. Put in another way, this means that the fact that the virus is in the leaf cells does not influence the time it takes to inactivate. Furthermore, the amount of irradiation to inactivate the virus within the leaf is distinctly larger than that necessary to kill the cells of the tobacco leaf.

Evidence presented earlier in this paper indicated that roentgen rays have their first noticeable effects on the chromatin structure of the cell or better on the genes contained within the chromatin, the effects on the cell as a whole coming as aftermath of gene changes affecting cell reproduction. Each cell has many of these genes. They are held together in groups by the chromatin matrix, the number of these groups being equal to the number of the chromosomes within the cells. Each gene has the size of large protein molecules. They are in pairs. The total number of these gene pairs within the cell is very large, 5,000 to 15,000 in some cells. The destruction of any one pair has been shown by Demerec[8] to be nearly always lethal to the cell. Besides the genes, the chromatin matrix is likewise subject to reorganization due to roentgen-ray absorption. These changes are also frequently lethal to the cell when the time for mitosis arrives. Thus, despite the fact that the individual genes are not large, their total number multiplied by their size makes a rather large total target for the roentgen rays to hit, the inactivation of even a small portion of which will immobilize the cell from further division.

In abnormal growths the cells must maintain their division rate to be dangerous. Such cells are at a distinct disadvantage when compared with those which may have ceased dividing and is acting as a purely mechanical supporting element. The destruction of any part of the inheritance structure in the first case would eliminate the abnormal cell by preventing its reproduction.

The question arises—why are not the observed effects of irradiating the *Drosophila* egg cytoplasm greater? The answer may lie in the physical size of the vital elements composing this material. Many of the molecules in the cytoplasm must be destroyed in irradiation. To be dangerous, however, the destruction of all of a vital kind is called for. The number of such elements in the cytoplasm, judging from such structures as the mitochondria, must be rather large. There is a rather wide margin of safety between any minimum number needed by the cell and the number normally present. Sufficient molecules are present so that the destruction of many more than two is necessary before the cytoplasm would be permanently impaired. Chemical considerations indicate that the size of these molecules is much less than that of the gene. The elements in the cytoplasm not only appear more numerous and

scattered than the genes, thus requiring more direct hits, but they also furnish a smaller target to absorb the energy. Considerations of probability show that the chance of making a cytoplasmic effect which will be lethal when a number of elements calling for several direct hits must be destroyed is less than where but two have to be changed as with each gene pair. The evidence above on the relation of size of target to roentgen effect likewise shows that the smaller sized objects of the cytoplasm would have less chance of inactivation under the same roentgen-ray dosage than would the large ones of the nucleus. The chance of making a lethal effect in the cytoplasm consequently appears definitely less than in the chromosome structure. The physical considerations involved in roentgen-ray absorptions are such that they may account for different cell elements showing qualitatively different inactivation rates.

SUMMARY

This paper discusses the interdependence of the inheritance structures and roentgen-ray effects in cell inactivation. The evidence presented indicates that the inactivation of *Drosophila* eggs by roentgen rays may possibly be largely accounted for by the absorption of energy within the gene and chromatin structure.

Virus particles, when in a liquid medium or when in the dry state, are inactivated by ultraviolet light or roentgen rays at similar rates, a fact which indicates a direct action of the radiant energy on the virus particles. The amount of radiant energy necessary to inactivate tobacco mosaic virus is large, so large as to make it doubtful if a cell could absorb sufficient energy to inactivate a virus contained within it and still survive.

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# A SCHEME OF PROTECTION WHICH HAS PROVED SATISFACTORY IN A LARGE RADIUM THERAPY CENTER

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THE re-housing in a new building of the Manchester and District Radium Institute, in connection with its incorporation with the Christie Hospital and Holt Radium Institute in 1933, made it necessary to consider most carefully the whole question of protection, so that once organized, the unit would be subject to the minimum amount of disorganization due to sickness of members of its staff, attributable to their association with radium.

Experience in the old Institute had shown very clearly that inadequate protection was accompanied by unhealthiness of the staff. During the latter part of 1932—the last period of work in the old Institute—the average white blood cell count of all workers was as low as 4,700. Very little protective equipment was in use, and the staff was so small that each individual had daily to receive a considerable amount of radiation. From September, 1934, onwards, with better working conditions, extensive use of protective screening, and a much larger staff, the average white blood cell count has been in the neighborhood of 6,000.

To me there fell the task of finding methods of rendering work in a radium department as little harmful as possible, and subsequently of establishing an adequate system of protection throughout the unit. It would appear that a description of a scheme of protection which has proved satisfactory in a large institute might be of help to others organizing protection in radium centers. In the following description dimensions of apparatus and constructional details are given where it is thought that these would be useful, and in most cases electroscopic measurements of the devices under working conditions are quoted. For these measurements, and for much assistance with the physical problems encountered in construction, I am indebted to the physicist, Mr. H. M. Parker.

The more usual means by which radium produces harmful effects in those who use it may be summarized thus:

(1) The introduction into the alimentary canal of radium salts either accidentally or as medicine.
(2) Breathing an atmosphere contaminated by radium emanation.
(3) Actual handling of radium or emanation, either free or in containers.
(4) Continuous or intermittent exposure of the body to radiation over a long period.

These items and the methods employed in combating their effects will be discussed seriatim.

(1) *Introduction into the Alimentary Canal.* The introduction of radium into the alimentary canal has produced clinically interesting, although often very tragic, results. Much of this radium is taken up by the skeleton, replacing calcium. The bones eventually become radioactive, and Martland and Humphries[1] have shown that about 92 per cent of this radioactivity is due to alpha radiation. Martland,[2] in describing the cases of the New Jersey luminous dial painters, also drew attention to the high incidence of bone sarcoma in those who survived the initial effects—some 27 per cent. Colwell and Russ,[3] and Gettler and Norris[4] have very fully reviewed both the problem of "radium as a pharmaceutical poison," and the literature upon the subject. As harmful effects from alimentary introduction of radium are not seen in therapeutic departments it was felt to be unnecessary to take any protective steps

against it, beyond a general warning of the danger of putting radium containers or contaminated gloves and instruments into the mouth.

(2) *Inhalation of Emanation.* The results of inhalation of radon are difficult to assess, because in practice general irradiation is taking place at the same time as the inhalation. The expired air of workers in pitchblende has been shown frequently to be radioactive, this radioactivity often being associated with a low blood count (McClelland[5]) in workers inhaling small quantities of radon over a period of several months. It would appear reasonable to expect similar findings in therapeutic workers but, so far, tests of expired air at the Holt Radium Institute have always given negative results.

The problem of protection against inhalation is essentially the general one of protection against harmful gases, and as such has been approached along the lines of prevention of leakage; provision of adequate ventilation; the formulation of rules of conduct in the event of accidental leakage, and the rendering unlikely of contamination of the main building and workrooms in case of serious accident to the plant.

In accordance with the recommendations of the International Protection Committee[6] the emanation plant is situated in the hospital grounds away from the main building. Its position is such that the prevailing winds blow the fan exhaust away from the hospital and workrooms. It is interesting that before the completion of the radon hut when the plant was housed in the main building for a time, radioactivity was discovered in the neighboring corridors when radon was being pumped. The emanation hut is built of wood and asbestos on a concrete base, the radium safe being a small brick and concrete "strongroom" abutting on one of the walls. If gross contamination of the hut takes place the latter may be completely destroyed and replaced by a room free from radioactivity at very little cost.

The radon plant in use is of the continuous tube type in which leakage is only likely to occur as the result of mistakes in operation of the valves, or actual breakage. In addition to three windows and the door, both impeller and suction fans are provided in the emanation hut, and are kept constantly running when it is occupied. The staff are given instructions that, should known leakage occur, the windows are to be widely opened, the room vacated for at least half an hour, and not to be used again until an electroscopic test has shown it to be safe to do so. The radon is sealed in the seeds or screens during its "inactive stage," before it leaves the emanation room. "Spent" radon screens are emptied of the glass capillaries in a special ventilated bench (which will be described later). The capillaries are buried in a "radon cemetery" in a far corner of the garden.

*Checks on Efficiency of Radon Protection.* Two checks are employed as routine. The room is examined with an electroscope, four times each year, and tests are made from time to time for radioactivity of the expired air of those working the plant.

(3) *Actual Handling of Radium.* In the early days of radium therapy, when treatments were much more often carried out by unscreened radiation, there were many cases of cracking finger nails, hyperkeratosis, fissuring of the skin, and in some cases epitheliomata were reported. Two of the technicians with longest service here show the effects of irradiation on their hands. Although with the increased use of metal-walled needles containing radium salts the problem became less serious, it was realized that the handling of emanation called for particular care of the hands, in view of the risk of actual contamination of them with radon, and consequent direct beta irradiation. Failla[7] states that probably everyone who works for a length of time with appreciable amounts of radium and particularly with radon, even under good conditions shows some slight finger effects. These may be merely occasional prickling sensations in the finger tips, a little roughening of the

skin, and a faint erythema or glossiness of the skin around the nails. When the individual ceases to be in contact with radium, however, these slight effects do not progress, and do in fact usually disappear. He adds that he has never known the skin of a technician to become worse, after leaving radium work, and lays down as a safe rule that if at the end of two years the radiation effects on the hands are limited to slight reddening and shiny appearance around the nails, as far as the *local* effect is concerned, a technician may probably work under the same conditions indefinitely. With regard to the supervention of malignancy, he draws attention to two important things: that, unlike in roentgen burns, epithelioma does not occur when the tissue has not been broken; that it may occur when breakdown of irradiated tissue is caused by subsequent trauma or septic infection.

*Method of Protection.* Protection of the hands is obtained by avoidance of actual contamination with radon, distance (of the order of a few inches), speed in handling, handling of radon only while "inactive," and avoidance of trauma to the hands at any time.

In handling radon, rubber gloves are worn, particularly while dismantling radon tubes, or manipulating the radon plant, but it is not the custom in the Radium Institute laboratories to wear them when manipulating radium element needles, it being felt that there is very little risk of primary beta contamination from these. Moreover, the use of gloves would cause a definite increase in the time taken to carry out the handling, thus increasing the general exposure to gamma radiation. Several types of special radium forceps have been tried out, but the technicians were found to be quicker using long, non-toothed dissecting forceps, covered with rubber tubing, and they unanimously preferred them. Special forceps are therefore not in general use.

The use of long-handled forceps in the work benches to give protection against beta radiation affords some slight gamma-ray protection also. Measurements made by wearing a film strapped to the back of the hand while silking needles with a wire silking device have shown as much as 1.5 r in an afternoon's work. It would appear that the only means of lessening this exposure easily is the division of the labor among as large a number of people as are available. This will be discussed later in reference to the general method of "division."

Members of the staff are warned from time to time of the necessity for general carefulness of their hands, and advised to remove all dirt, and rub in lanoline after any mechanical "tinkering" either at work or at home.

*Checks on the Efficiency of Hand Protection.* Examination of all the workers' hands is undertaken every three months. A written description is kept of their condition at each examination, and photographs for subsequent comparison are added in cases where there is visible damage. Actually there have been no new cases of radiodermatitis recently, but, as already stated, two of the workers who were in the service of the Institute in the early days, when there was little protection, have some degree of skin damage. Probably the old type of radon plant involving the collection of the gas at two stages over beehive shelves was an important causal factor in these cases.

(4) *General Irradiation.* Protection against general gamma irradiation is by far the most important part of the problem of rendering radium work reasonably safe. Gamma-ray effects fall naturally under three headings:

(i) Effect on reproductive system.
(ii) General effect.
(iii) Effect on blood.

(i) *Effect on Reproductive System.* Protection is along lines similar to that of the blood. It has been shown physiologically on several occasions that the protection in the Radium Institute is adequate from this point of view.

(ii) *General Effect.* Workers after heavy exposure often complain of tiredness and inability to concentrate, out of proportion to the physical exertion expended. Protection against general exposure is described in the section on blood effects.

(iii) *Effect on Blood.* The effect on the blood is the chief problem. Workers show blood changes very early in their association with radium. Most authorities agree that the earlier changes begin during the first few weeks, marked leukocytic oscillations frequently occurring during this period. Within a few months practically all workers develop a leukopenia, due to a reduction in the circulating neutrophiles,[8] the red count on the other hand being slightly lower than the individual's previous "normal." A fatal anemia of aplastic type may develop.

It would appear to be desirable that any scheme of protection should be based upon knowledge of the maximum amount of radiation which does not produce serious harmful effects. Unfortunately, this is not definitely known for gamma rays, but the International Protection Committee,[9] acting on the experience of years, has fixed an intensity of $10^{-5}$ r/sec. (a daily dose of 0.2 r per working day of seven hours), as being safe for roentgen-ray work. This figure has been used as a basis in designing protective apparatus against both roentgen and gamma rays in the Radium Institute.

*Methods of Protection Against General Irradiation.*

These may be classified under the following headings:

(i) Distance.
(ii) Working conditions.
(iii) Speed in working.
(iv) Lead protection devices.

(i) *Distance.* This is the cheapest and most effective form of protection. It applies both to the question of general gamma irradiation in distances of the order of a few meters, and to the beta-ray hand problem in distances of a few centimeters.

(a) *The Building.* The new building was planned with protection in view. It is single storied so that there are no rooms above or below the radium safe or workrooms. The making-up room and the mould room are separated by cloakrooms and a telephone kiosk. The room in which radium is mounted on applicators is separated from the mould room by a corridor. Thus the only radium close to a worker is that which he is actually handling. The mould room and making-up laboratory are big rooms, with large windows facing southwest. An electrical fan and system of vents in the workbenches give adequate ventilation in the latter.

The radium safe is housed in a small strong room near enough to the making-up room to avoid long exposure in transport, but far enough not to be a source of danger to the making-up room, from which it is separated by two 9 in. brick walls and a corridor 3 ft. 6 in. wide.

(b) *Instructions to Staff.* Radium workers are instructed that only the individual actually carrying out an operation should be near the radium, and that others must not congregate in the make-up room while radium is being handled.

(ii) *Working Conditions.*

*Rotation and division of duties and short-term service.*

(a) *Rotation.* In radium centers with large staffs it is possible to arrange that each technician only takes duties entailing a large amount of irradiation for relatively short periods, separated by longer intervals of either very limited irradiation or actual non-exposure, during which he is still a useful servant. In the Radium Institute it has been the custom to rotate the technician monthly between the radium safe and the making-up laboratory, wherein considerable exposure is to be expected, and the manufacture of moulds in the mould room, where none is taken.

(b) *Division.* Similarly medical work can readily be divided not only in terms of arduousness of work, but so as to apportion the exposure equally between the medical staff. If the staff is sufficiently large this division is a very effective protective meas-

ure. The principle of division has been applied fairly easily to the medical staff because the work of a large institute involves many necessary medical duties that do not entail the handling of radium. For example, the daily follow-up clinic provides full employment for two doctors every morning. During 1936 a total number of 2,713 radium treatments was carried out. The exposure involved was divided among eight doctors. Thus, in 1936 each doctor averaged 0.9 treatments involving exposure per day. This figure should be compared with the average of 1.2 treatments per day during 1934 when with the protection, as at present, the blood counts were abnormal. The lay staff has been increased from three in 1932 to seven in 1936.

(c) *Short-term Service.* In the past lay workers have been retained for a number of years on the rotary basis. Recently it has been felt that the possible minimal exposure per person, even with a comparatively large lay staff, is sufficiently high to render short-term service safer. This gain in safety outweighs any considerations of the unfairness of insecurity of employment. It appears that radium laboratory work must be considered as "dead-end" employment when the major issue of permanent physical damage is contrasted with the social problem of "no prospects." The present policy of the Institute, therefore, is to employ technicians for a maximum of two years' service, rotating their duties during their term of employment.

(d) *Holidays.* The International recommendations with regard to the one month holiday per year, and the five seven-hour days per week, are carried out as routine.

(iii) *Speed.* Speed lessening the time of close proximity to sources of radiation plays an important part in protection. Only practice gives real facility in the use of the hands, and it takes a new technician a little time to learn to work quickly. This was one of the main arguments in determining the old policy of employing an almost permanent lay staff.

Speed has been assisted by the provision of good natural and artificial lighting; unobstructed direct vision through large windows in the work-bench lids; benches with arm holes at the correct width apart; adjustable stools, giving a comfortable working position for any worker; the provision of lead blocks in which to hold needles or vaginal corks during silking or filling; small wire threading tools for silking; and the avoidance of any clumsy, or intricate instruments or forceps.

(iv) *Lead Protection Devices.* The actual handling of radium necessitates the curtailment of the beneficial remoteness to which reference has already been made, so that it becomes necessary to insert, between the worker and the radium, screens which absorb radiation. Lead is the most economical screen, comparing bulk and efficiency with price. Various minor difficulties were encountered when the purchase of lead was undertaken. The lead must be pure lead—"lead" used for many commercial projects is, of course, not pure lead, the necessary degree of hardness having been obtained by the addition of other metals.

It is unwise, therefore, to obtain "lead" by melting down old piping or tanks. New lead is sold as "commercial lead" and "chemical lead,"—the latter being practically of analytical pureness and slightly more expensive. Both have been found quite suitable for the construction of lead screens to absorb roentgen and gamma rays.

Protection apparatus can be built up in various ways:

(1) *Complete Lead Castings.* These are, of course, free from joint leakage. They are, on the other hand, clumsy to move if changes are made. They are more expensive to buy initially, and to alter subsequently if they are not suitable in their original form. Their efficiency may be impaired by serious "blow-holes." Very little apparatus has been constructed on this plan in the Institute, it being felt that the one advantage of freedom from leakage was outweighed by the many disadvantages.

(2) *Small Lead Bricks.* These small units

of lead, about 1×2×3 in., originally suggested by Dr. Burrows (the first Medical Officer in Charge of the Institute) may very readily be built up into protective screens. While they have the very definite disadvantage of forming walls with many crevices through which leakage may occur, they have many advantages. They are less expensive than castings; they are easily altered in layout; they may be cut out from rolled sheet lead (free from "blow-holes") —most of these in the Radium Institute were made by this method. When not in use they may be readily stored in odd corners. A stock of these "bricks" is kept for use in all temporary, or experimental layouts.

(3) *Slabs—either Cast or Rolled.* Castings were found to be subject to the disabilities of casting in general. The advantages of rolled slabs, however, are numerous. They are free from blow-holes; they give flexibility of shape; they offer an uninterrupted surface of protection in the place in which this is required. Apparatus may be so built that the crevices are "open" only in directions away from the worker. If any crevice at all is undesirable, they may be fused together *in situ*. They were found to offer the cheapest efficient method of constructing lead protective apparatus, and have been used for most of the permanent screens in the Institute.

## DESCRIPTION OF LEAD PROTECTIVE APPARATUS

(1) *Safe.* Four and a quarter grams of radium element are stored in the safe, which in turn is housed in a concrete strong room. The construction of the radium holding portion was fully described by Walmsley[10] in 1931. Briefly a framework of square-section gunmetal tubes, each holding a lead-filled brass drawer, is surrounded by lead blocks to a thickness of 6 in. The chief advantage of this type of construction is that, up to the cubic capacity of the safe itself, additional drawers may be added as further radium is acquired, without incurring great expense, and without loss of protection. On several occasions such additions have been made.

Of importance in the everyday use of such a safe, are the provision of strong handles to the drawers, and the limitation of their movement by safety catches. Good lighting in the safe helps to reduce the time taken to remove or replace radium. It was found that a black-stained shallow wooden trough, placed below the safe door, served the dual purpose of preventing technicians standing too close to the safe, and needles dropping on the floor and rolling into inaccessible positions. The contents of the drawers are not labelled on the front, as this might give rise to avoidable exposure in peering at the writing. Instead, a plan of the drawers with their contents clearly specified upon it is situated immediately outside the safe room.

*Efficiency of the Safe.* In compiling these data it has been assumed that there were 1,500 mg. in the safe—about the average amount not in clinical use at one time.

(a) Immediately outside safe-room door intensity considerably less than $10^{-5}$ r/sec.

(b) All drawers closed, but safe door open, abdomen of a worker standing by the safe gets $0.54\times10^{-5}$ r/sec.

(c) Worker removing radium from a drawer containing 200 mg. (an unusually large amount) approximately $10\times10^{-5}$ r/sec. He would need to do this for over two hours to receive daily tolerance dose.

(2) *Lead Boxes.* At all points in the hospital where radium has to be idle, lead boxes are provided.

(a) *Making-up Laboratory.* In the making-up laboratory is a large lead box in which radium that has been silked ready for use may be stored safely till called for. It is fitted with a Yale lock so that it may be used as a reception box during week-ends, or holiday times when the department is officially closed, and the main-safe keys are not available (see Fig. 1).

It is built up of 2 in. thick slabs of lead arranged so as to have the three walls abutting into the laboratory 4 in. thick, the wall to the corridor 2 in. thick, and a 2 in. floor.

The lid is 1 in. thick, and is carried in a counterbalanced iron frame to prevent sagging, and to make handling easy. Its internal dimensions are 12 in. broad, 15 in. long, 10 in. deep. The whole structure is mounted on concrete so that the top is 3 ft. 6 in. from the floor, thus affording maximum protection over the abdomen and chest of those using it.

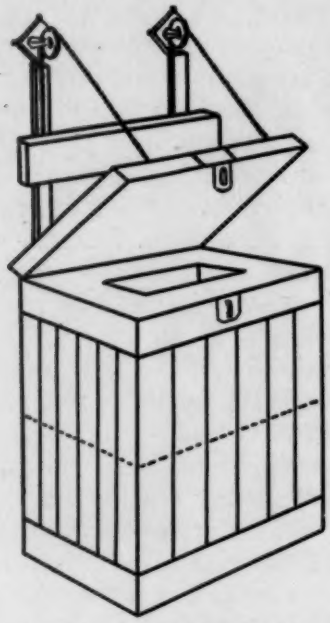

Fig. 1. Lead box in making-up laboratory.

*Efficiency of Subsidiary Safe in Laboratory*. Contents 500 mg. radium element.

Lid closed $0.4\times10^{-5}$r/sec. close up to box.

Lid open $0.75\times10^{-5}$r/sec. close up to box.

It thus offers a safe resting-place in readily accessible position for radium awaiting transmission, the 500 mg. used in the test being about the maximum contents at any one time.

(b) *Wards*. On each ward unit a wooden box lined with 1 in. of lead and mounted 3 ft. from the floor is provided for the storage of radium moulds, or needles, which have been removed from patients at times when the radium office is closed. These boxes are erected in the small test-room away from the ward for the protection of the nursing staff, and are fitted with Yale locks to ensure the safety of the radium. It is improbable that they do in fact play any important part in the protection of the nursing staff, as they never contain more than a very small proportion of the radium in the ward. It would appear that the freedom from blood changes among the nurses is mainly due to the use of lay staff in the making-up and mould laboratories, and the use for radium work of not more than 50 per cent of the beds in any ward. The "radium beds" are those at the far end of the ward away from the drug cabinet, desk, and sluice rooms, where nurses spend most of their time.

(c) *Operating Theaters*.

(i) *Theater Work Box*. A lead box mounted on a trolley is provided for the use of the nurse in the operating theater. Its internal measurements are $10\times4\times6$ in. high, and its walls are 2 in. thick. A perforated detachable copper lining is fitted inside. The carrying blocks containing the radium are placed in this lining, and boiled in the radium sterilizer. When the doctor is ready to begin treatment of his case, a sterile towel is placed over the box, and the copper lining containing the radium dropped into it, taking the center of the towel down into the box with it, and draping the rest of the towel over the box and upper part of the trolley (see Fig. 2). The nurse carries out the loading of the forceps, and the insertion of catgut for stitching, with the radium actually in the lead box. The maximum amount of radium in the box at one time for a breast implantation does not exceed 150 mg. with which quantity daily tolerance dose would be reached in two hours. In practice, of course, the quantity is falling throughout the treatment so that the average amount of radiation received by the nurse is very much less. Furthermore, it only takes about three-quarters of an hour to carry out a breast implantation. The doctor's irradiation is slightly greater than the nurse's, he receiving maximum amount, however, at the end of the treatment when most of the radium is in the patient.

That this work box was a wise provision is borne out by the fact that the doctor receives most of his radiation in the operating theater. In 1932, with no theater protection, each doctor carried out 339 treatments, and the average white blood cell count fell to 4,700. In 1936 the average treatment per doctor was exactly the same, but theater protection was in use, and the white blood cell count was just under 6,000. Kaye, Bell and Binks[11] have shown that an operator using 100 mg. of unprotected radium takes 0.25 r in the region of his abdomen in one-quarter hour!

(ii) *Steam-operated Lead-walled Radium Sterilizer.* Nurses must spend some time in the sterilizing room attached to the theater in order to prepare the instruments and bowls for use, apart from the actual sterilizing of radium. For their protection, a lead-walled, steam-operated sterilizer has

Fig. 2. Lead work box for operating room (exploded diagram).

been fitted in the sterilizing room. It is a cast-lead box with 2 in. sides, and a 1 in. floor and lid. The latter is, of course, counterbalanced. The inside dimensions are 16×11×11 in. high, although a perforated detachable copper-lining slightly reduces these. When 300 mg. of radium is being sterilized in it, a person would need to stand close up to it for three hours to receive daily tolerance dose to the abdomen. In practice it is unnecessary to be within several feet of the sterilizer, except when actually putting radium in or out (see Fig. 3).

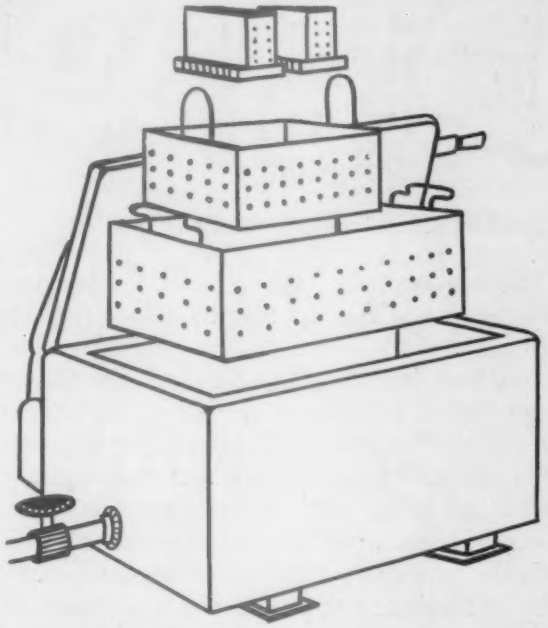

Fig. 3. Lead-walled sterilizer for operating room (exploded diagram).

(3) *Lead Work Benches.* Wherever radium has to be made up, or dismantled, or put into applicators, lead work benches have been provided. The simplest type of lead L-bench, using 1 or 2 in. thickness of lead, was found to be unsatisfactory for general use, as its openness led to its abuse. It was found that for a work bench to be effective it must not only afford the requisite lead screen to trunk and thighs, but that it must also be comfortable to work at, be well lighted and be sufficiently enclosed to preclude working over the top of it. A further point which seemed of importance was that it should be unnecessary to remove radium from it in order to carry out any usual procedure; it is worth while having a sink, hot and cold water, a bunsen burner, and a good electric light inside the bench. Lead glass windows afford so little protection against gamma rays and are so

expensive that they were considered to be unnecessary.

The basis of all lead work benches in the Manchester Radium Institute is a lead L.

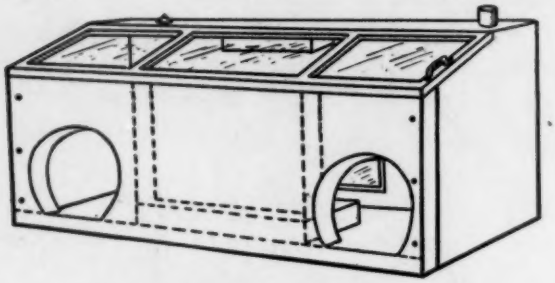

Fig. 4. Lead work bench for laboratories.

The earlier ones had 1 in. lead sides and floors in addition to this to afford protection to others in the small rooms of the old Institute, but later benches had the rest of the "box" completed in wood, the larger rooms in the new building making it possible to make use of the cheaper, and equally effective benefits of remoteness.

A typical work bench is constructed as shown in Figure 4. Swivel chairs, adjustable for height are provided for workers at the benches.

(4) *Lead Carrying Devices.*

(a) *Radon Seed Pots* (Fig. 5). These are cylindrical containers made of 1 in. lead with a lid giving 1 in. of protection, yet

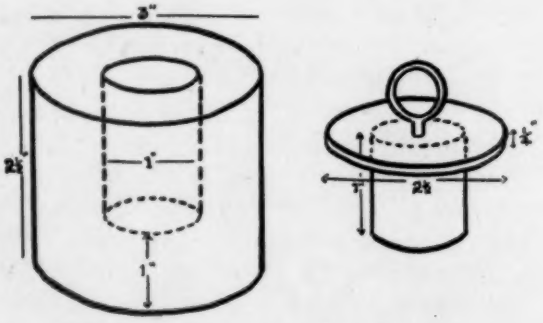


Fig. 5. Lead radon seed container.

affording ample room for 50 seeds or more. These "pots" are put into the sterilizers and the seeds boiled up in them. The nurse subsequently loads the gold seed gun from them behind a 1 in. lead bench. Under these conditions a person may handle 50 mc. for one and a half hours before daily tolerance dose is reached. This does not in practice happen in the Institute as most of the cases treated with gold seeds only require about 10 mc. each. The protection is thus quite adequate when it is borne in mind that the nurse is exposed to 10 mc. for two to three minutes on about six occasions one afternoon per week. The nurse doing this work does not have any other exposure.

(b) *Carrying Blocks* (Fig. 6). These are lead blocks $9.5 \times 6 \times 3$ cm. enclosed in zinc, and having a piece of slotted rubber at the base to hold the needle silks. Two parallel lines, each of ten vertical holes, are

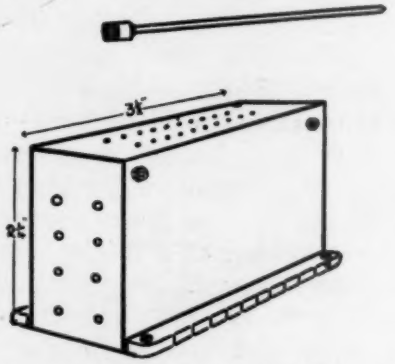


Fig. 6. Lead carrying block for needles and tubes.

drilled into them to hold the needles. Through each line of holes a number of holes are bored crossing them at various heights. Through these a brass rod may be pushed, in order to make the blocks suitable for carrying needles of different lengths. Each block weighs 3½ lb., and provides a minimum of ½ in. of lead protection. Measurements show that whereas at a certain distance 200 mg. of radium without protection give $20 \times 10^{-5}$ r/sec., if this radium is carried divided between a number of lead carrying blocks, it gives only $2 \times 10^{-5}$ r/sec. under otherwise similar conditions—only one-tenth as much.

*The Radium Office.* The checking of radium both on its inward and outward journeys should be done behind a lead screen, but it is not desirable that the porters of radium should have access to the

making-up room, or to the safe. To overcome this objection, and yet protect the staff, a special radium receiving and issuing office was incorporated in the new building. It has a booking-office type of window, opening in the main corridor. Behind this window is a 2 in. lead L-bench, electrically lighted from above, upon which radium is counted.

*Transport of Radium.* This falls naturally into two groups, that within the hospital, and to other hospitals.

(a) *Internal Transport.* The radium is made up in the lead carrying blocks just described, and these in turn are carried in long-handled boxes. The boxes are lined with 1 cm. of lead, and are of such a size that they will just hold 5 lead blocks. The radium is then wheeled about the hospital in long-handled trucks. Toy trucks made of wood (obtained from a toy store) with extended handles holding the radium 140 cm. from the porter are used. Gradients on the main corridor made it impossible to use lead trolleys—although one or two experimental ones were constructed. The radium needles are carried in lead containers in a long-handled carrying box in the trolley. That the method is reasonably efficient is borne out by the fact that it takes three hours for daily tolerance dose to be given to the abdomen of a porter conveying radium.

Financially, there is no comparison between the use of distance and that of lead for protection for transport purposes. The wooden truck with its extended handle costs about four dollars.—Quotations were in the region of seventy-five dollars for a mechanically efficient and radiologically safe lead trolley.

Radium is returned from the wards and theater to the radium office by nurses. Long-handled boxes without lead are used for this, as experience has shown that excessive weight makes the nursing staff dispense with all protection, and just carry the radium around in a kidney-dish or bowl, generally clutched tightly to their chests to protect the radium. Each ward has a suitable box allotted for its own use, and the radium curator is not permitted to accept radium in the radium office which has been transported carelessly.

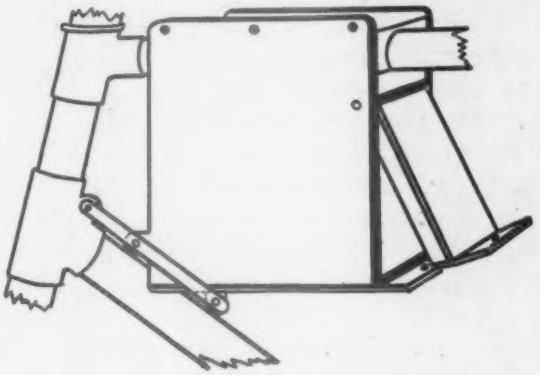

Fig. 7. Lead container for carrying radium on bicycles.

(b) *External Transport.* The Institute provides radium service to a number of Voluntary and Municipal Hospitals in Lancashire, Cheshire and Denbighshire. Radium has to be carried distances that involve exposure to quantities up to about 0.5 gram for one and a half or two hours. Wherever possible, arrangements have been made for the outside hospitals to provide transport, generally in their own ambulance. The exposure is then taken by casual labor, and the size of the vehicle makes it possible to keep the radium at a safe distance from the driver. Unlined boxes with locks are used, though the radium itself is in lead carrying blocks.

In order to facilitate the conveyance of radium from local hospitals where the use of a motor vehicle would be unwarranted, a carrying box for attachment to ordinary pedal bicycles has been constructed. This takes the form of a brass box, of such dimensions as to hold a carrying block modified to hold 40 needles, yet not injure the knees of the cyclist. It is clamped to the front end of the crossbar, and stayed from the lower tube. The door and padlock are at the back in full view of the rider. Lead protection of 1 cm. is provided at the top and in the door. The box weighs 6½ lb. empty, and 10 lb. with the carrying block.

*Efficiency of Cycle Carrying Box* (Fig. 7). Carrying 200 mg.—an unusually large, though possibly necessary, amount. With radium loose in the box, the rider's abdomen is exposed to 0.3 r/hr. Radium in its carrying block in the box, the figure is 0.05 r/hr. The usual journey made by this box takes one-half hour.

When the radium has to be taken by a member of the Institute medical staff, it is carried in lead-lined boxes similar to those used in the hospital. At 2 ft. it takes about one hour for daily tolerance dose to be delivered when carrying 300 mg. of radium. It is not usually possible to get the radium farther than 3 ft. away from the driver of a normal sized motor car, except by using the luggage grid at the back. The weight of the lead and the value of the radium discourage the use of this otherwise useful accessory. The more modern car bodies with enclosed luggage compartments behind the rear seats greatly reduce this difficulty. For example, a 114 in. wheelbase car of well-known make has a luggage compartment at the rear, approached by a hinged panel at the back. The driver receives seven times as much radiation from radium carried in the rear floor as he does from the same quantity carried in the luggage compartment.

*Methods Employed in Checking the Efficiency of Protection.* Three main checks on the efficiency of the protective methods in use are employed in the Institute. They are regular blood counts of the staff, periodical examination of the hands of the staff, and the testing of workrooms for radioactivity.

(a) *Regular Blood Counts.* These give by far the most important check available. The blood of all workers, medical and technical, is examined at the time of their appointment, and subsequently at intervals not exceeding one month during the time of their service. Goodfellow[8] as research hematologist, has brought forward evidence to show that different individuals differ in their susceptibility to the effects of irradiation; that whereas the more sensitive exhibit at first lymphocytosis with neutropenia on overexposure, the less sensitive show lymphocytopenia with a monocytosis. Only one sign of overexposure was common in the blood counts of all workers examined in the Institute—a leukopenia due to a reduction in the number of circulating neutrophiles. This sign has more recently been taken as being diagnostic of overexposure, and in cases where it has occurred steps have been taken to ascertain and remove the cause.

(b) *Periodic Examination of Hands of Staff.* The hands of all new members of staff are examined on their appointment. They are subsequently examined three times a year, and a record is kept of the results of this examination. One employee, who worked for many years in the old Institute, shows definite skin changes, and photographs of these are taken and filed from time to time to enable changes to be appreciated more readily.

(c) *Checking Room for Radioactivity.* In any department in which large numbers of radon seeds or needles are used a certain amount of leak and loss of radon are bound to occur. About twice a year all workrooms in the Institute are subjected to a test for radioactivity. Originally this was carried out with a gold leaf electroscope, but more recently a Geiger counter type of instrument of the type described by Chalmers[12] has been used.

## DISCUSSION

There can be no doubt from the low average white blood cell count of both lay and medical workers in the old Institute that protective devices are necessary in any institution where radium work is carried out. It is also clear that the provision of extensive protective apparatus and rules has rendered it possible for each individual to carry out the same amount of work as before, and yet maintain a white blood cell count at a level which, although possibly slightly under his normal, does not appear to affect his health.

Very extensive protective equipment has been installed in the new Institute. It is

difficult to assess accurately just how much of this equipment is actually necessary, and how much of it merely makes assurance doubly sure. As members of the medical staff handle radium only in the operating theater it must be to the protection equipment there that improvement in their white blood cell count is due. It would appear then that the provision of adequate lead screening in the operating theater and sterilizing room is essential.

Lay technicians receive radiation in "making-up" the radium, putting it in and out of the safe, attaching it to moulds, and during its transport. Adequate lead screening is only feasible for making-up, and attaching to moulds. The improvement in health must then be attributed partly to lead screens and partly to the general principles of division and rotation.

A good solution of the transport problem would appear to be the use of casual lay porters such as ambulance drivers, and hospital porters from outside hospitals seldom using radium. Sufficient lead screenage for doctors to be responsible for their own long-distance transport is too cumbersome to be practicable.

Special measures for the protection of the nursing staff in the wards have never been shown to be necessary in this Institute, probably because nurses take no part in the preparation of radium or the manufacture of radium moulds. The lead boxes for radium awaiting use certainly do not make any serious contribution to their safety, for they never contain beyond a very small proportion of the radium in the ward.

SUMMARY

(1) Protective rules and equipment in the Christie Hospital and Holt Radium Institute are described.

(2) Measurements of their efficiency are given.

(3) It is shown from the blood counts of the staff that great improvements have been effected.

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# A STANDARDIZED RADIUM TUBE—RELATED DOSAGE PROBLEMS

## PRELIMINARY NOTE

*By* J. MURDOCH, *Professor of Radiology, University of Brussels*, ROBERT COLIEZ, *Electro-radiologist of the Paris Hospitals*, AND ERNEST STAHEL, *Professor of Physics, University of Brussels*

AT THE Fourth International Congress of Radiology at Zürich, we proposed the adoption of a standard radium tube with the object of simplifying dosage in radium therapy.[8] This standard tube would be used for all current applications in intracavitary therapy (e.g., cancer of the cervix) or for external therapy with small radium-skin distance (1–5 cm.). It is not intended at the moment to extend this standardization to radium beam therapy (telecurietherapy) nor to interstitial radium treatment. The standardization of needles used for interstitial radiation would be very desirable, but at the present this problem must be reserved for future study.

In order to establish the basis of an international agreement, we intend to examine in this paper the general principles governing the choice of a standard radium tube and to discuss the technique of measuring the distribution of radiation in the vicinity of this tube.

### A. CHARACTERISTICS OF THE STANDARD TUBE

(1) *The Radium Content of the Tube Should Be Expressed in Milligrams of Radium Element.* It is unnecessary to discuss why this notation has been definitely adopted; it has practically superseded notations expressing radium content in terms of sulphate or bromide of radium.[4]

(2) *The Standard Tube Should Contain 10 mg. of Radium Element.* This amount of radium content is commonly adopted in France, Belgium and Switzerland,[1] and is convenient both as regards internal and external treatment. As the object of selecting a standard tube is to fix the values of isodose curves in the vicinity of the tube, there is no point in preserving any longer the complicated values of 6.66 mg. and 13.33 mg. which were used only to enable comparison to be made with radon tubes, now almost obsolete.

Besides this standard 10 mg. tube, a similar tube containing only 5 mg. would be provided for the reason that in planning a radiation treatment it is necessary to dispose of tubes containing different quantities of radium, so as to obtain homogeneity of the radiation field. This 5 mg. tube would have the same length and the same filtration as the standard tube, but its diameter would be slightly inferior; the corresponding isodose curves could easily be obtained from those of the standard tube.

To distinguish the 5 mg. from the 10 mg. tubes in routine work and to avoid serious mistakes, it is recommended that the 5 mg. tube be gold plated, the 10 mg. tube having the silvery appearance of platinum.

(3) *The Standard Tube Should Be Made of Platinum.* Although silver, copper and lead are still in use in some countries, platinum-iridium is used almost exclusively in Sweden, Belgium, Czecho-Slovakia, Switzerland, and other places. This metal possesses the great advantage (especially as regards internal therapy) of providing a heavy filtration for a fairly small thickness.

(4) *Dimensions of the Standard Tube.* First of all, the active length and wall thickness of the tube have to be determined. Most radium centers use tubes having a wall thickness of 1 mm. and an active length of 15 mm. These dimensions comply with the requirements of radium therapy and there is no need to alter them. Filtration of less than 1 mm. platinum is less and less employed, except perhaps in Germany and the United States. Particular attention should be paid to Regaud's

suggestion that the radium be packed in a thin-walled cell (0.1 mm. Pt) and this cell placed inside a sheath 0.9 mm. thick. This precaution would make it possible, in case of accident, to recover more easily and more completely the precious element.

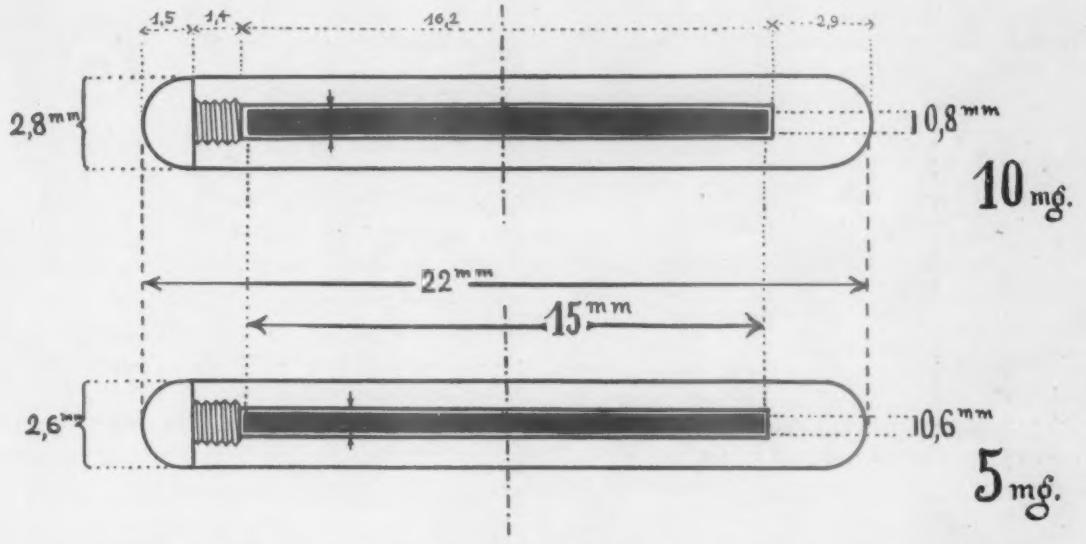


Fig. 1. Proposed dimensions for standard tubes of 5 and 10 mg. radium element. The lengths of tubes are equal; only the active diameter is different.

The dimensions of the sheaths indicated below are such that a small cell of this kind can be packed into it.

The diameter of the sheath is determined by the volume necessary to accommodate the radium without leaving any empty spaces. This corresponds to an internal diameter of 0.8 mm. for 10 mg. and 0.6 mm. for 5 mg., allowing for the wall thickness of the cell. This small difference in the internal diameters is insignificant as far as the shape of the isodose curves is concerned. The external diameter of the standard 10 mg. tube would therefore be 2.8 mm., while that of the 5 mg. tube would be 2.6 mm.

The ends of the tube must also have a definite form. They should be exactly similar, so that the isodose curves may be symmetrical. It is not necessary that the thickness of the extremities be equal to the lateral wall thickness; as a matter of fact, the rays which pass through the ends of the tube undergo additional filtration by reason of the length of radium traversed and because of the obliquity of their path through the walls near the end of the tube. The resulting minimum on the isodose curves at the end of the tube is unavoidable. Moreover, the technical requirement of filling and soldering the tubes necessitate a screw plug, 3 mm. in length, at one of the ends. The other end must have the same thickness for reasons of symmetry. This arrangement accentuates the minimum which exists in this direction, but this may be taken into account in the measurement of the isodose curves and entails no difficulties in practice. The eyelet of the tube should be abolished since it is no longer required and merely creates an asymmetry in the isodose curves (Fig. 2). The total length of the standard tube would therefore be 22 mm. (Fig. 1).

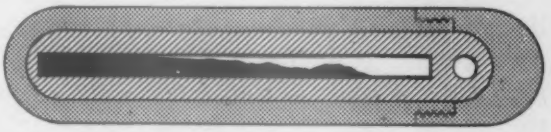

Fig. 2. Asymmetry in a tube of bad design, due to the presence of an eyelet and to defective filling.

In conclusion, the proposed standard dimensions are:

| | 10 mg. Radium Element | 5 mg. Radium Element |
|---|---|---|
| Active length | 15 mm. | 15 mm. |
| Active diameter | 0.8 mm. | 0.6 mm. |
| Wall thickness | 0.9 mm. +0.1 mm. (cell wall) =1 mm. Pt | 0.9 mm. +0.1 mm. (cell wall) =1 mm. Pt |
| Total length of tube | 22 mm. | 22 mm. |
| External diameter of tube | 2.8 mm. | 2.6 mm. |

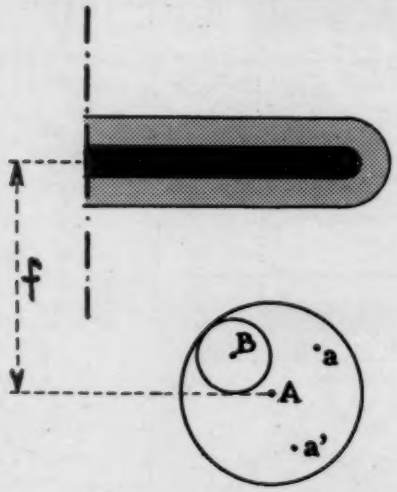


FIG. 3. When too large an ionization chamber is used, the isodose curves close to the tube cannot be correctly determined.

(5) *Sheaths for Supplementary Filtration.* Certain radiotherapists use sheaths for extra filtration, corresponding for the most part to a thickness of 1 mm. platinum (Proust and Mallet, Delporte and Cahen, Ostrcil). The modifications of the isodose curve due to the use of such sheaths can be determined. In practice, the shape of the curves remains unaltered and it suffices to introduce a reduction factor appropriate to the thickness of the supplementary sheath.

These sheaths are generally made of platinum-gold alloy. To prevent mistakes, some distinctive mark should be put on sheaths for the 10 mg. tubes. For instance they should be marked with a plainly visible number, or provided with a silver band, or even be silvered all over. The sheaths for the 5 mg. tubes could retain their golden appearance, the same as the 5 mg. tubes themselves.

### B. DETERMINATION OF ISODOSE CURVES

The measurement of the radiation in the vicinity of radium tubes was hampered for many years by the lack of a suitable technique. For one thing, the insufficient protection of the conductors joining the ionization chambers to the electroscope caused appreciable errors in the measurements. Moreover, the volume of the ionization chambers (some of which exceeded 1 cc.), while capable of giving integrated values, did not permit precise measurement in the immediate vicinity of the radium tube, at the very place where the isodose curves crowd together, and where the intensity gradient is steepest. When such a chamber of large volume is used, the center of the chamber (*A*, Fig. 3) cannot approach sufficiently close to the surface of the tube; certain parts of a large chamber, such as *a*, are overdosed, while regions such as *a'* are distinctly underdosed in relation to *A*; the

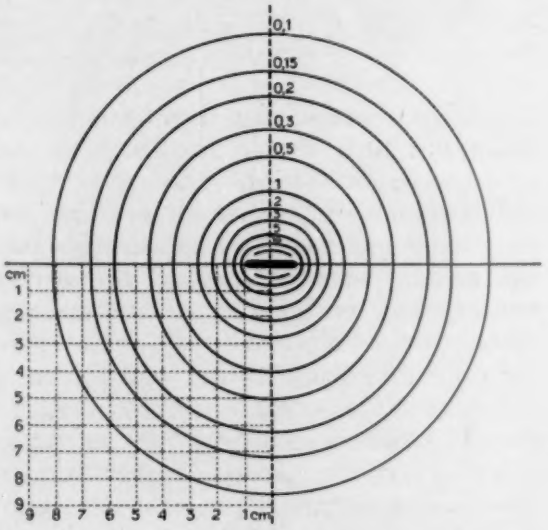


FIG. 4. Isodose curves for a tube of standard dimensions, filter 1 mm. Pt, supposed filled with 1 mg. radium element. The doses are expressed in international roentgens (after Stahel).

summation of the total ionization does not give the exact ionization at point *A*. The decrease of the intensity of the isodose curves is incorrect; the larger the ionization chamber, the more the intensity gradient is smoothed out.

To obtain a proper measurement of the distribution of radiation around the radium standard tube, the following conditions must be observed:

(1) The measurement *must be carried out in water*, the radium tube being placed under conditions identical with those of therapeutic practice.

(2) The ionization chamber employed must be of small dimensions and its volume must not exceed 2 mm.$^3$, at least for exploring the first 20 mm. from the tube axis.

An ionization chamber of this description[12,13] has been in use at the Brussels University Tumor Center since 1929.

(3) The ionization chamber should show no appreciable directive effect, i.e., the ionization current should be independent of the orientation of the chamber with respect to the tube axis, and should depend only on the relative position of the geometrical center of the chamber and the tube.

(4) It is of great advantage if surface applicators used in transcutaneous therapy can be measured or calculated before their application. Such a determination can be made with the help of a small exploring chamber which integrates the radiation received from all the tubes, or by a method of integration using the isodose curves. The latter method has been in use at the Brussels University Tumor Center since 1930.[2,3,5,6,7,9,10,11]

Purely as an illustration, we give here an isodose curve in roentgens, measured by Stahel, for a tube of standard dimensions (1 mg. of radium element, filter 1 mm. Pt). It is easy to calculate the doses for a tube containing other quantities of radium: 5 or 10 mg. for instance, or even for the older tubes of 6.66 mg. and 13.33 mg. The isodose curves for a 5 mg. and a 10 mg. tube, having the same active lengths, are identical in shape, within the errors of measurement.

Our object in proposing the adoption of a standard radium tube is to simplify dosage, and to make possible comparison of the therapeutic results of different clinics. We submit our proposal to the Permanent Committee of Dosage of the International Congress of Radiology and also to the League of Nations Committee for Radiotherapy of Cancer.

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# SOME STUDIES ON THE DIELECTRIC STRENGTH OF INSULATING FLUIDS*

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THE insulation problem is of major consideration in the design of roentgen-ray generating apparatus, as it plays so important a rôle in determining the minimum size and weight which can be realized in such equipment of a given rating. This attainment of minimum size and weight is obviously important in all roentgen-ray generating outfits which are movably mounted. It is also important in very high voltage generators which may otherwise call for special buildings to house them.

The problem of controlling the critical behavior of the insulating material and maintaining constancy of its insulating strength becomes increasingly important and difficult as one designs roentgen-ray units for still higher voltage. When one has arrived at a suitable design of generator for a certain high voltage, one might make the assumption that a satisfactory design for a higher voltage unit could be reached by increasing the linear dimensions. Even if this assumption were correct and the linear dimensions were doubled for twice the generating voltage, the volume would be increased eight-fold. Before making such a rapid increase in volume in building supervoltage units, one should go as far as possible in improving the properties of the dielectrics that are used. With this thought in mind the following studies and observations may be of interest.

Many years ago Natterer[1] found that the insulating properties of different gases and chemical vapors vary widely. Interest in this field was awakened recently by Joliot, Feldenkrais and Lazard's[2] report that the output voltage of their electrostatic generator was doubled by saturating the surrounding air with carbon tetrachloride at room temperature.

In our laboratory we have been investigating recently the effect of various factors on the dielectric strength of a number of gases, gas-vapor mixtures and liquids.† This study included a determination of the relative dielectric strengths of several gases and of nitrogen saturated with various vapors. In these experiments the comparative values of dielectric strength were measured with respect to nitrogen at room temperature and a pressure of one atmosphere. The relative dielectric strength is defined as the ratio of dielectric strength of the gas or nitrogen-vapor mixture to that of nitrogen at atmospheric pressure and room temperature, when measured in the same gap.

In most of this work we have used nickel disk electrodes 1 inch in diameter, having the faces rounded to spherical surfaces of 2-inch radius, and with electrode spacings ranging from $\frac{1}{8}$ to $\frac{1}{4}$ inch. In special cases a pointed tungsten wire opposed to a flat nickel disk has been used. The test voltage was supplied by a voltage doubling circuit giving a maximum d.c. voltage of 60 kv. with a negligible ripple.

To speak first of the gases and vapors, we have studied the electrical properties of carbon tetrachloride under a variety of conditions with a point-to-plane combination of electrodes. The change in appearance of the corona discharge upon addition of carbon tetrachloride to nitrogen is very marked indeed.[3] With nitrogen the visible discharge from a pointed electrode (anode) consists of relatively long tenuous stream-

* Read at the Fifth International Congress of Radiology, Chicago, Ill., Sept. 13–17, 1937.

† For a complete account of this work, published after this paper was prepared, see "Dielectric strength of insulating fluids," E. E. Charlton and F. S. Cooper, *General Electric Rev.*, 1937, *40*, 438.

TABLE I

RELATIVE DIELECTRIC STRENGTHS OF VARIOUS GASES AND NITROGEN-VAPOR MIXTURES

| Gas or $N_2$-Vapor Mixture Saturated at 23° C. and 760 mm. Hg Total Pressure | Pressure of the Vapor (mm. of Hg Absolute) | Boiling Point (°C.) | Molecular Weight | Heat of Formation (Kilocalories per Mol.) | Relative* Dielectric Strength |
|---|---|---|---|---|---|
| $CCl_2F$ | 725 | 24.1 | 137.36 | | 3.0 |
| $C_2Cl_2F_4$ | 760 | 3.8 | 170.91 | | 2.8 |
| $C_2Cl_2F_2$ | 306 | 47.2 | 187.37 | | 2.6 |
| $CCl_2F_2$ | 760 | − 28. | 120.91 | | 2.4 |
| $BCl_3$ | 760 | 12.7 | 117.19 | 88.3 | 2.3 |
| $CH_3I$ | 370 | 42.35 | 141.95 | − 4.5 | 2.2 |
| $SO_2$ | 760 | − 10.0 | 64.06 | 70.92 | 1.9 |
| $PCl_3$ | 113 | 76. | 137.39 | 70.0 | 1.9 |
| $SOCl_2$ | 110 | 75.6 | 118.97 | 42.7 | 1.65 |
| $CCl_4$ | 105 | 76.74 | 153.83 | 25.9 | 1.65 |
| $CHCl_3$ | 180 | 61.28 | 119.38 | 23.6 | 1.58 |
| $CH_3COCl$ | | 50.92 | 78.48 | 60.9 | 1.57 |
| $SO_2Cl_2$ | | 69.1 | 134.97 | 80.8 | 1.56 |
| $Cl_2$ | 760 | − 34.6 | 70.91 | | 1.55 |
| $CS_2$ | 330 | 46.3 | 76.12 | −26.1 | 1.50 |
| $C_2H_5ONO_2$ | | 88.7 | 91.05 | 33.4 | 1.47 |
| $CCl_3COCl$ | | 118. | 181.83 | | 1.40 |
| $CHCl_2F$ | 760 | 14.5 | 102.92 | | 1.33 |
| $H_2S$ | 760 | − 60.75 | 34.08 | 5.3 | 1.30 |
| $C_2H_4$ | 760 | −103.9 | 28.03 | −11.0 | 1.21 |
| $TiCl_4$ | 12 | 135.8 | 189.73 | 172.4 | 1.17 |
| $HCOOCH_3$ | 570 | 31.50 | 60.03 | 84.9 | 1.16 |
| $CHCl:CCl_2$ | 65 | 86.60 | 131.38 | | 1.15 |
| $N_2O$ | 760 | − 89.5 | 44.02 | −19.65 | 1.14 |
| $POCl_3$ | 34 | 108. | 153.39 | 138.4 | 1.11 |
| $CH_2Cl_2$ | 400 | 39.95 | 84.93 | 21.7 | 1.11 |
| $C_2H_2$ | 760 | − 83.6 | 26.02 | −53.9 | 1.10 |
| $CH_3Cl$ | 760 | − 24.4 | 50.48 | 20.1 | 1.06 |
| $(CH_3)_2NH$ | 760 | 7.4 | 45.06 | 8.2 | 1.04 |
| $CH_2ClF$ | | | 68.47 | | 1.03 |
| $CO$ | 760 | −191.59 | 28.00 | 26.84 | 1.02 |
| $CHCl_2CHCl_2$ | 6.8 | 146.20 | 167.84 | 33. | 1.02 |
| $S_2Cl_2$ | 12.5 | 137.1 | 135.03 | 5.65 | 1.02 |
| $CH_3Br$ | 760 | 3.7 | 94.94 | 8.5 | 1.02 |
| $(C_2H_5)_2O$ | 495 | 34.60 | 74.08 | 60.† | 1.00 |
| $C_2H_5OH$ | 52 | 78.32 | 46.05 | 56.95 | 1.00 |
| $C_6H_5COCl$ | est. 0.2 | 197.3 | 140.50 | 54.† | 1.00 |
| $CH_3COCH_3$ | 210 | 56.13 | 58.05 | 62.† | 0.98 |
| $CH_2(CH_2)_4CHCl$ | | 142.5 | 118.54 | | 0.98 |
| $C_6H_5Br$ | ca. 4 | 156.15 | 156.96 | | 0.93 |
| $C_6H_5CHCl_2$ | | 214. | 160.96 | | 0.93 |
| $CCl_2:CCl_2$ | ca. 18 | 121.20 | 165.83 | − 6.0 | 0.91 |
| $CH_3(CH_2)_4CHBr$ | | 165.5 | 163.00 | | 0.88 |
| $CO_2$ | 760 | − 28.5 | 44.00 | 94.45 | 0.88 |
| $C_6H_5NH_2$ | ca. 0.3 | 184.3 | 93.06 | − 5.5† | 0.87 |
| $(C_2H_5)_4Pb$ | | | 323.35 | | 0.85 |
| $C_6H_6$ | 85 | 79.7 | 78.05 | −20.3 | 0.84 |
| $NH_3$ (over $NH_4OH$) | | | 17.03 | 11. | 0.82 |
| $C_6H_5Cl$ | 10.5 | 131.69 | 112.50 | | 0.81 |
| $CH_3NH_2$ | 760 | − 6.79 | 31.05 | 7.3 | 0.81 |

* The relative dielectric strength is defined as the ratio of dielectric strength of the gas or nitrogen-vapor mixture to that of nitrogen at atmospheric pressure and room temperature, when measured in the same gap.

† Calculated from heat of combusion data in International Critical Tables.

ers. Upon the addition of carbon tetrachloride vapor, the corona streamers disappear and the discharge is confined to a very short intense blue glow which persists almost unchanged until complete breakdown occurs in the form of an intense white spark. As with nitrogen, visible corona commences at a lower voltage when the pointed electrode of a point-to-plane combination is negative. With this arrange-

ment the voltage for spark breakdown in nitrogen is increased approximately threefold by saturating the nitrogen with carbon tetrachloride at room temperature and atmospheric pressure. The voltage at which corona begins is raised but little as if the vapor served principally to stabilize the corona discharge. Corona is suppressed in the same general way if the pointed electrode is made the cathode. Between spherical electrode surfaces there was no evidence of corona preceding spark breakdown with any of the gases tested.

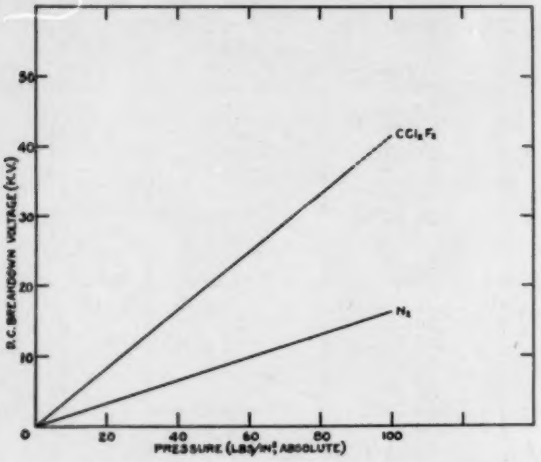


FIG. 1. Variation of breakdown voltage with pressure for $CCl_2F_2$ and for $N_2$ measured successively with the same electrode arrangement.

The relative dielectric strength of nitrogen-carbon tetrachloride mixtures was studied as a function of concentration of the vapor. The relative dielectric strength increased most rapidly at very low concentrations of the vapor, reached a value of 1.65 at a molecular concentration of 14 per cent corresponding to saturation at 23°C., and became about 3.2 for pure carbon tetrachloride at 80°–85°C., a temperature slightly above the boiling point of carbon tetrachloride.

Nitrogen-carbon tetrachloride mixtures were tested up to a total pressure of 200 lb. per sq. in. absolute and room temperature with an excess of liquid carbon tetrachloride in the pressure cell. The dielectric strength of the mixture at any given total pressure and room temperature was greater than that of nitrogen alone at the same pressure, but the ratio of these dielectric strengths decreased from 1.65 at atmospheric pressure to 1.3 at 80 lb. per sq. in. and to about 1.2 at 200 lb. per sq. in. This behavior can be explained by the decrease in molecular concentration of carbon tetrachloride as the total pressure is increased.

Relative dielectric strength measurements were made on a variety of other vapors and gases. These were chosen to test the effects of such variables as electron affinity, molecular weight, heat of formation and the choice and arrangement of certain radicals, double bonds, etc., within the molecule. In Table 1 are listed several of these compounds in order of decreasing relative dielectric strength as measured in a corona-free gap. For liquids with boiling points above room temperature, the vapor pressure is as important a factor in determining the measured values as are the inherent properties of the vapor molecules.

Some generalizations may be suggested, at least for the compounds investigated. Most materials with high relative dielectric strengths contain halogens or sulphur, although the presence of these compounds does not insure high dielectric strength. Certain groups of atoms such as the amine group and the benzene ring seem to be definitely detrimental. Molecular weight is not a controlling factor. The degree of correlation with heat of formation is not particularly suggestive. The dielectric strengths of compounds closely related chemically may vary widely.

One of the above compounds which seems well fitted for high voltage insulation is dichlorodifluoromethane. It is colorless, odorless, non-poisonous, non-corrosive and is stable chemically and electrically. The curve of breakdown voltage versus pressure is linear up to 90 lb. per sq. in., the vapor pressure at 23°C., and has a slope greater by a factor of about 2.5 than the similar curve for nitrogen as shown in Figure 1. In addition, its high vapor pressure at room temperature facilitates its use

in high pressure applications. Thus at 90 lb.per sq. in. (abs.) dichlorodifluoromethane has a relative dielectric strength that is 15.3 times greater than nitrogen at atmospheric pressure, and at atmospheric pressure it is 2.5 times greater than nitrogen at the same pressure. For pressure above 90 lb. per sq. in. an inert gas such as nitrogen could be added to any desired total pressure. The variation of dielectric strength with molecular concentration of a mixture of dichlorodifluoromethane and nitrogen (Fig. 2) at a total pressure of one atmosphere was found to be nearly linear. The approximate dielectric strength of this mixture at higher pressures, as shown in Figure 3, can be calculated easily, assuming a linear increase of dielectric strength with pressure. Thus, for example, the calculated dielectric strength of nitrogen saturated with dichlorodifluormethane at room temperature and 200 lb. per sq. in. absolute pressure is 24.8 times greater than it is for nitrogen alone at atmospheric pressure. As seen from the curves in Figure 3, dichlorodifluoromethane at 90 lb. per sq. in. pressure, the vapor pressure at 23°C., is 1.92 times greater in dielectric strength than is nitrogen saturated with carbon tetrachloride at 90 lb. per sq. in. pressure and 23°C.

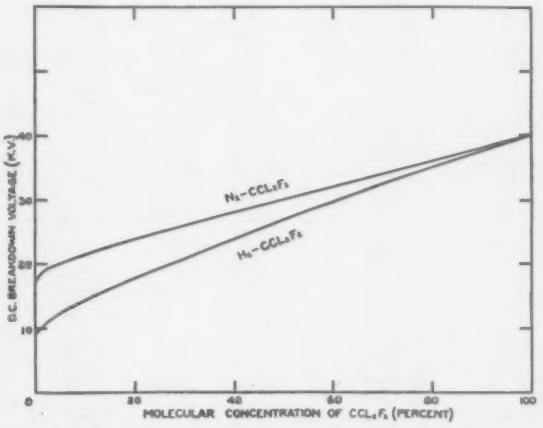


Fig. 2. Dependence of breakdown voltage on concentration of $CCl_2F_2$ in $N_2$ and in $H_2$. Total pressure, 1 atm.; temperature, 23°C.

Mixtures of dichlorodifluoromethane and hydrogen (Fig. 2) also give an almost linear relation between dielectric strength and molecular concentration. The dielectric strength increases by a factor of about 4.4 upon complete replacement of one atmosphere of hydrogen by one atmosphere of dichlorodifluoromethane. A disadvantage of the mixture of this material with hydrogen is the corrosive nature of the by-products produced by an electric discharge.

For applications requiring a comparatively low total pressure, dichlorotetrafluoroethane may be a more desirable insulating medium than dichlorodifluoromethane. It has a vapor pressure at room temperature of about two atmospheres, absolute, thus permitting use of the saturated vapor over the liquid phase. At this pressure its relative dielectric strength is 5.6 as compared with 5.0 for dichlorodifluoromethane.

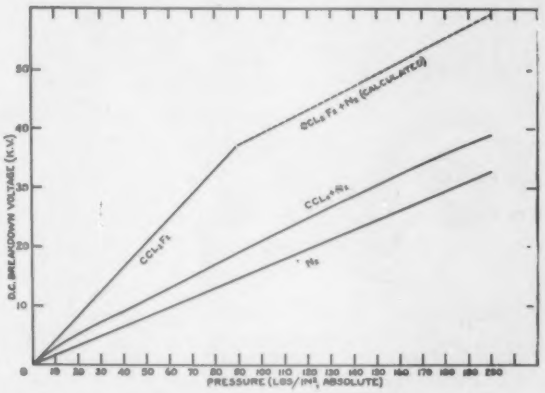


Fig. 3. Variation of breakdown voltage with pressure for $N_2$ and for mixtures of $N_2$ with $CCl_4$ and $CCl_2F_2$. Temperature, 23°C.

While dichlorodifluoromethane and dichlorotetrafluoroethane offer worthwhile gains where pressure is permissible, trichloromonofluoromethane gives a somewhat greater gain when operation at atmospheric pressure is desirable. It has good physical properties and a relative dielectric strength of about 3.0. Table II summarizes the relative dielectric strength data comparing dichlorodifluoromethane, trichloromonofluoromethane, dichlorotetrafluoro-

ethane, and nitrogen-carbon tetrachloride mixtures with nitrogen at atmospheric pressure and room temperature.

Thus, the dielectric strength of dichlorodifluoromethane is 2.5 times that of nitrogen; the dielectric strength of dichlorotetrafluoroethane is 2.8 times that of nitrogen; the dielectric strength of a nitrogen-trichloromonofluoromethane mixture is 3.0 times that of nitrogen; and that of a nitrogen-carbon tetrachloride mixture is 1.65 times that of nitrogen alone at room temperature and atmospheric pressure.

TABLE II

RELATIVE DIELECTRIC STRENGTHS OF SOME METHANE AND ETHANE DERIVATIVES UNDER VARIOUS CONDITIONS OF TEMPERATURE AND PRESSURE

| Compound | Temperature (°C.) | Pressure of the Vapor (atmospheres, absolute) | Relative Dielectric Strength |
|---|---|---|---|
| $CCl_2F_2$ | 23 | 6.05 | 15.3 |
| | 23 | 1 | 2.5 |
| $CCl_3F$ | 23 | 0.95* | 3.0 |
| $C_2Cl_2F_4$ | 23 | 2 | 5.6 |
| | 23 | 1 | 2.8 |
| $CCl_4$ | 80 (approx.) | 1 | 3.2 |
| | 23 | 0.14* | 1.65 |

* In $N_2$ to a total pressure of 1 atm.

Table III summarizes the gain in dielectric strength to be had by the addition of dichlorodifluoromethane and of carbon tetrachloride to nitrogen at total presssure of 90 and 200 lb. per sq. in.

If one goes to 90 lb. per sq. in. total pressure of nitrogen at room temperature, the dielectric strength of nitrogen is increased 6.1 times over atmospheric pressure. If one saturates the nitrogen with carbon tetrachloride at 90 lb. per sq. in. total pressure, the dielectric strength of the mixture is 7.9 times nitrogen at atmospheric pressure, and if one replaces the nitrogen with dichlorodifluoromethane at 90 lb. per sq. in. total pressure, the dielectric strength of this gas is 15.3 times nitrogen at atmospheric pressure. The calculated relative dielectric strength of the nitrogen-dichlorodifluoromethane mixture is 24.8 at a total pressure of 200 lb. per sq. in.

Whereas dielectric strength tests for gases normally give reproducible breakdown voltages for a given electrode arrangement, an entirely different situation usually holds in the case of tests on liquid dielectrics. An occasional dielectric failure of the liquid insulation may occur at voltages far below the average values determined by dielectric strength measurements. These low values rather than the much higher average values determine the practical design of a high voltage unit. A tremendous amount of effort has been made over a long period of years by many investigators not only to improve the quality of insulating liquids but also to learn more about the mechanism of dielectric breakdown and evaluate the various factors involved.[4] Today, we still find divided opinion as to the breakdown mechanism and the principal contributing causes of insulation failure. However, there is much experimental evidence that the breakdown strength of the insulating materials can be still vastly improved, especially in totally enclosed systems.

TABLE III

RELATIVE DIELECTRIC STRENGTHS OF $N_2$ AND $N_2$-VAPOR MIXTURES AT ELEVATED PRESSURES

| Gas or Vapor Mixture | Temperature (°C.) | Vapor Pressure (lb. per sq. in. absolute) | Total Pressure (lb. per sq. in. absolute) | Relative Dielectric Strength |
|---|---|---|---|---|
| $N_2$ | 23 | | 90 | 6.1 |
| $N_2+CCl_4$ | 23 | 2.03 | 90 | 7.9 |
| $N_2+CCl_2F_2$ | 23 | 90 | 90 | 15.3 |
| $N_2$ | 23 | | 200 | 13.6 |
| $N_2+CCl_4$ | 23 | 2.03 | 200 | 16.2 |
| $N_2+CCl_2F_2$ | 23 | 90 | 200 | 24.8* |

*Calculated.

In applying dielectric strength data on liquids to the design of high voltage roentgen-ray equipment one may find it incorrect

to assume that by doubling the linear dimensions the breakdown voltage will be doubled also. In addition to such a variation of gradient with spacing some of the other factors which have been found to play a rôle in determining the voltage gradient at which breakdown in a liquid dielectric will occur and which makes extrapolated data doubtful are the following: chemical constitution, water content, gas content, fiber or solid particle contamination, electrode shape, electrode spacing, surface condition of electrodes, material of electrodes, rate of increase of measuring voltage, frequency of measuring voltage, duration of application of voltage, and the total voltage impressed.

In our studies with an oil-immersed roentgen-ray unit designed for operation at 500,000 volts,[5] 5 inches of liquid oil insulation is used in the region where the maximum difference of potential exists. If we were to extrapolate the dielectric strength test data obtained with this oil when placed in a standard 1/10-inch gap, it should be capable of withstanding 3,000,000 volts. If no particular efforts are made to remove air from the unit while it is being filled with oil, the trapped air bubbles may be responsible for a breakdown of the insulation across this 5-inch gap occurring below 300 kv. (peak). The presence of solid particles such as fibers suspended in the oil may decrease the strength of the oil even more than gas bubbles. If the fibers are dry they do not appreciably affect the insulating value of the oil, but if they are wet they will very markedly decrease its breakdown strength. This is probably due to the high dielectric constant and high conductivity of this wet material which concentrates in the field where the stress is greatest. The spread in breakdown values that may be obtained for a given liquid across a fixed gap when repeated many times is possibly to a great extent due to changing amounts of gas, water and solid material that may be present in the region of greatest stress when the breakdown tests are being made.

While much can be done in general high voltage design by better distribution of the voltage stress throughout the liquid insulation, even more might be accomplished by improving the breakdown strength of the liquid itself. This improvement may come not only by a suitable choice of the insulating liquid but also by an adequate treatment to reduce the amount of trapped gas, water and solid suspended materials in the liquid insulation in the assembled roentgen-ray unit.

While it would not be possible to keep water, air and foreign particles out of an open tank, the oil immersed type of roentgen-ray outfit can be tightly closed, if necessary hermetically sealed, and therefore makes possible the exclusion of such contaminants. This permits more rigid control of the physical and chemical properties of the enclosed conducting and insulating materials. It also prevents the escape of vapors.

The dielectric strength of liquids may also be materially improved by increased pressure.[6] If we test the dielectric strength of some clean, gas-free insulating oil in an enclosed system so arranged that we can vary the pressure on the gas-free oil up to 200 lb. per sq. in., we find that the average dielectric strength of the oil has been increased approximately 50 per cent by the increased pressure. If the same kind of pressure tests are made with insulating oil that has not been made gas-free, one still finds some gain in the dielectric strength with increased pressure, but to a lesser degree. The use of a compressed liquid for insulation permits one to retain the advantage of its cooling properties. Compressed gas or vapor dielectric, on the other hand, introduces a new problem in connection with the removal of heat from the different parts of the transformer. This can be accomplished, however, in various ways.

Few general conclusions can safely be drawn and the extent to which any of the above experiments and observations prove of interest will depend upon the specific application to which they are made. More exact knowledge concerning the mechanism

of breakdown in insulating fluids will enable us to do a better job in the selection, treatment and application of these insulating materials.

Most of the data published in the literature on the breakdown strength of insulating fluids have been taken with short gaps. A great deal of the data we have described was also obtained with short gaps and with comparatively low total voltage applied.

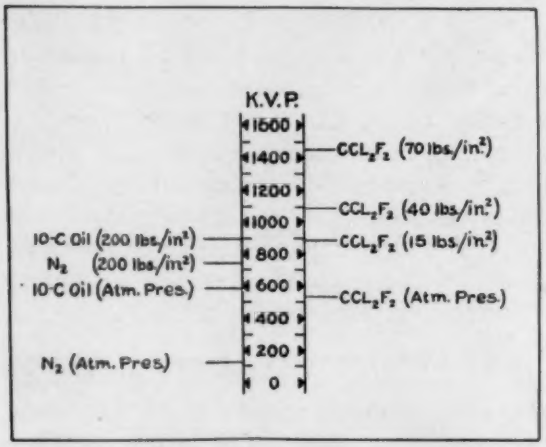


FIG. 4. Maximum operating voltage of a high voltage roentgen-ray transformer using various insulating fluids.

We are now preparing to repeat some of these tests at very high voltages by placing a high voltage transformer in a pressure tank and testing the dielectric strength of different insulating fluids at various pressures up to 200 lb. per sq. in. and with gaps large enough, so that possible total test voltages up to 1,500 kv. (peak) may be used.

Some preliminary data illustrating the comparative dielectric strengths of different insulating fluids when used at various pressures in a high voltage transformer are shown in Figure 4. This figure clearly shows the relative effectiveness of nitrogen, oil and dichlorodifluoromethane as insulating media for a particular high voltage roentgen-ray transformer. It also demonstrates the spread in operating voltage that can be obtained by the use of various insulating materials.

As a result of such studies, one may possibly build roentgen therapy units capable of producing roentgen rays of very short wave length which are of relatively small volume and weight, thus readily permitting their installation and use in existing hospital buildings.

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# THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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# EDITORIAL

## SUBDURAL HEMATOMA

THE clinical syndrome of subdural hematoma has been known for a long time, and in recent years there has grown up a voluminous literature on the subject. Not only are there reports concerning the hematoma that occurs in adults as a result of trauma, but a number of articles on subdural hematoma in infants have been recorded. Traumata to the head during birth and infancy occur fairly frequently and, as has been shown by a number of authors, subdural hematoma occurs much more frequently at this time than is ordinarily believed.

Recently Davidoff and Dyke[1] have called attention to a condition which they term "relapsing juvenile chronic subdural hematoma." Their description is of a group of cases showing subdural hematoma originating apparently in early childhood, continuing without symptoms during adolescence and suddenly becoming reactivated following another trauma. Their report is based on a group of four cases occurring in patients at the ages of six, fourteen, sixteen and eighteen years. In a study of the plain roentgenograms of the skulls of these patients, they discovered a number of variations from the normal skull on the side of the lesion. These changes varied in degree from one case to the next and were not all present in every case but were similar in kind. The changes which they noted consisted of "(1) elevation of the sphenoid ridge, superior orbital plate, and superior orbital ridge, (2) deepening, widening and lengthening of the middle fossa, (3) disappearance or indistinctness of the oblique line delineating the postero-lateral wall of the orbit, (4) atrophy of the inferior and lateral wall of the superior orbital fissure, (5) hypertrophy of the frontal and ethmoidal sinuses, and (6) thickening of the skull." In their report they illustrate the mechanism of these changes with the clinical histories of the four cases.

In addition to the changes which are observed on the ordinary roentgenograms of the skull, the pneumo-encephalograms revealed in this group of cases normal-sized ventricles, slight or moderate displacement of the ventricles to the side opposite the lesion, relatively slight asymmetry of the lateral ventricles and relatively slight difference in the roofs of the lateral ventricles. These encephalographic changes, Davidoff and Dyke observed, are unlike those seen in the chronic subdural hematomas occurring in adults after a single injury.

As an explanation for the bone changes observed in the skulls of this type of case, Davidoff and Dyke suggest that there is primarily increased intracranial pressure by the original hematoma chiefly exerted locally upon the wall of the middle and anterior fossa laterally and the neighboring brain medially. This pressure must be exerted for a sufficient time to result in the ballooning or expansion of the relatively malleable skull of the child and associated atrophy of the brain, and secondarily, decreased intracranial pressure subsequent to resorption of fluid from the sac of the hematoma which results in hypertrophy of the accessory nasal sinuses and thickening of the cranial vault. Previously they have called attention to these secondary changes in the skull and sinuses occurring as a result of cerebral atrophy or hypoplasia in cases of infantile hemiplegia.

These changes observed in the skull are quite naturally the result of long standing pathological processes but the immediate

[1] Davidoff, L. M., and Dyke, C. G. Relapsing juvenile chronic subdural hematoma; a clinical and roentgenographic study. *Bull. Neurol. Inst. New York*, 1938, 7, 95–111.

symptom which brings the patient to the hospital is that of some recent trauma which results in fresh bleeding and re-expansion of the old hematoma. It must be some mechanism such as this, reason Dyke and Davidoff, as the changes in the skull are of too pronounced a degree to be the result of a recent trauma, and they emphasize the importance of going quite minutely into the history of the patient when such bone changes as are observed in the skull of these cases are evident at the original study. It is a well recognized fact that chronic subdural hematoma is a disease occurring more often in adults, especially males, as a result of their more frequent exposure to trauma, but the frequent reports in the literature suggest that the disease is also common in early childhood. Davidoff and Dyke, however, point out the fact that the occurrence of subdural hematoma during adolescence has received too little attention and they suggest that the condition is quite common during the adolescent period. It is of importance, therefore, to recognize these skull changes in all cases exhibiting intracranial symptoms and particularly is it of importance to recognize the relatively slight but very definite changes which might be observed in the pneumo-encephalograms. In the light of Davidoff and Dyke's observations and experience in this group of cases, there seems justification for the use of the term "relapsing juvenile chronic subdural hematoma."

# SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

*Items for this section solicited promptly after the events to which they refer.*

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*Secretary*, Dr. C. B. Peirce, Royal Victoria Hospital, Montreal, Canada. Annual Meeting: Chicago, Ill., Sept. 19–22, 1939.

**AMERICAN COLLEGE OF RADIOLOGY**
*Secretary*, Dr. E. L. Jenkinson, 1439 S. Michigan Ave., Chicago, Ill. Annual meeting, 1939: To be announced.

**SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION**
*Secretary*, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: St. Louis, Mo., May 15–19, 1939.

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**INDIANA ROENTGEN SOCIETY**
*Secretary*, Dr. C. C. Taylor, 23 E. Ohio St., Indianapolis, Ind. Meeting held the second Sunday in May annually.

**LONG ISLAND RADIOLOGICAL SOCIETY**
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**MILWAUKEE ROENTGEN RAY SOCIETY**
*Secretary*, Dr. S. A. Morton, Columbia Hospital, Milwaukee, Wis. Meets monthly. Place of meeting named by the president.

**MINNESOTA RADIOLOGICAL SOCIETY**
*Secretary*, Dr. H. M. Weber, Mayo Clinic, Rochester, Minn.

**NEBRASKA RADIOLOGICAL SOCIETY**
*Secretary*, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets first Wednesday of each month, at 6 P.M., at either Omaha or Lincoln.

**NEW ENGLAND ROENTGEN RAY SOCIETY**
*Secretary*, Dr. A. O. Hampton, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

**RADIOLOGICAL SOCIETY OF NEW JERSEY**
*Secretary*, Dr. W. J. Marquis, 198 Clinton Ave, Newark, N. J. Meets annually at time and place of State Medical Society. Mid-year meetings at place designated by the president.

**NEW YORK ROENTGEN SOCIETY**
*Secretary*, Dr. R. D. Duckworth, 170 Maple Ave., White Plains, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

**NORTH CAROLINA ROENTGEN RAY SOCIETY**
*Secretary*, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

**CENTRAL NEW YORK ROENTGEN RAY SOCIETY**
*Secretary*, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year—January, May, November.

**PACIFIC ROENTGEN CLUB**
*Secretary*, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

**PENNSYLVANIA RADIOLOGICAL SOCIETY**
*Secretary*, Dr. L. E. Wurster, 416 Pine St., Williamsport, Pa. Annual meeting, May, 1939. Exact time and place to be decided.

**PHILADELPHIA ROENTGEN RAY SOCIETY**
*Secretary*, Dr. B. R. Young, Temple University Hospital. Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St

**PITTSBURGH ROENTGEN SOCIETY**
*Secretary*, Dr. H. W. Jacox, 4800 Friendship Ave., Meetings held second Wednesday each month, 4:30 P.M., October to June at various hospitals.

**ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.**
*Secretary*, Dr. S. C. Davidson, 277 Alexander St., Meets on second Thursday from October to May, inclusive, 8 P.M., Rochester Academy of Medicine Building.

**ST. LOUIS SOCIETY OF RADIOLOGISTS**
*Secretary*, Dr. W. K. Mueller, University Club Bldg. Meets fourth Wednesday of October, January, March and May, at a place designated by the president.

**SAN FRANCISCO RADIOLOGICAL SOCIETY**
*Secretary*, Dr. L. H. Garland, 450 Sutter St., San Fran-

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

cisco. Meets monthly on first Monday at 7:45 P.M., alternately at Toland Hall and Lane Hall.

South Carolina X-Ray Society
*Secretary*, Dr. Hillyer Rudisill, Jr., Roper Hospital, Charleston. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

Tennessee Radiological Society
*Secretary*, Dr. F. B. Bogart, 311 Medical Arts Bldg. Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
*Secretary*, Dr. H. C. Harrell, 517 Pine St., Texarkana, Texas. Next regular meeting in Temple, Texas, 1939.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
*Secretary*, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00–5:00 P.M., Room 301, Service Memorial Institute.

Virginia Radiological Society
*Secretary*, Dr. V. W. Archer, University Hospital, University, Va. Meets annually in October.

### Cuba

Sociedad Cubana de Radiologia y Fisioterapia
*Secretary*, Dr. Francisco Padron, Enrique, Villuendas 64, Havana, Cuba. Meets monthly in Havana.

### British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets on the third Thursday of each month, from November to June inclusive, at 8:15 P.M., at 32 Welbeck St., London, W. 1, or as advertised.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine, 1, Wimpole St., London, W. 1.

Section of Radiology and Medical Electricity, Australasian Medical Congress
*Secretary*, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
*Secretary*, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to Nov. incl. for scientific discussion.

Canadian Association of Radiologists
*Secretary*, Dr. A. C. Singleton, Medical Arts Bldg., Toronto, 5, Ontario.

Section of Radiology, Canadian Medical Association
*Secretary*, Dr. C. M. Jones, Inglis St., Ext., Halifax, N.S.

Radiological Section, New Zealand British Medical Association
*Secretary*, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

### Continental Europe

Belgian Society of Roentgenology
*Secretary*, Dr. J. Boine, Avenue des Alliés, 134, Louvain (Belgium).
Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Sociedad Espanola de Radiologia y Electrologia
*Secretary*, Dr. J. Martin-Crespo, Fuencarral, 7, Madrid, Spain. Meets monthly in Madrid.

Société de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
*Secretary* for French language, Dr. A. Grosjean, La Chaux de Fonds.
*Secretary* for German language, Dr. Scheurer, Molzgasse, Biel.
Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale
Meets monthly on fourth Tuesday, except during month of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
*Secretary*, Dr. Walter Altschul, German University, Prague, 11.52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.
*Permanent Secretary*, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Süd- und Westdeutsche Röntgensellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Röntgengesellschaft
Meets annually in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the Spring, and one in the fall.

Societa Italiana Radiologia Medica
*Secretary*, M. Ponzio, University of Turin, Prof. Turin

Societatea Romana de Radiologie si Electrologie
*Secretary*, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania.
Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
*Secretaries*, Drs. S. A. Reinberg and S. G. Simonson, Meets annually.

Leningrad Roentgen Ray Society
*Secretaries*, Drs. S. G. Simonson and G. A. Gusterin.
Meets monthly, first Monday at 8 o'clock State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
*Secretaries*, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky.
Meets monthly on the first Monday at 8 o'clock, the place of meeting being selected by the Society.

Polish Society of Radiology
*Secretary*, Dr. Jan Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
*Secretary*, Dr. B. Krynski, 11 Zielna St.
Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime:

Society of Medical Radiology in Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
*Secretary*, Dr. G. Biering, Copenhagen.
Meets the second Wednesday of each month from October to July in Copenhagen, at 8 o'clock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Roentgen Society
Meets first Wednesday of each month, at 6:30 P.M. at Zentral-Röntgen Institut des allgemeinen Krankenhauses Alserstrasse 4.

### Orient

Japan X-Ray Association
c/o Orthopedic Surgery, Tokyo Imperial University. Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto Japan. Meets bi-monthly on third Sunday.

## BULLETIN OF THE INTER-SOCIETY COMMITTEE FOR RADIOLOGY

From time to time activities by local radiological groups or county and state medical societies result in important contributions to the general welfare of radiology. Such is the report, reprinted below, which was adopted by the Medical Society of New Jersey at the 1938 session of its House of Delegates. Entitled "Supplementary Report Relating to Hospital Insurance," the report was prepared by the Auxiliary Medical Services Committee of the state society. Dr. William W. Maver, Jersey City, was chairman.

For a clear analysis of the problems arising in hospital-radiologist relationships and a definite proposal for solution, the report is worthy of study by radiologists and medical societies in other states. In future issues of the Inter-Society Committee Bulletin, important projects of interest to radiology in other localities will be reported.

Deleted of special sections devoted to pathology, anesthesia, and physical therapy, the full report, as approved by the Medical Society of New Jersey, follows:

Throughout its deliberations, as well as in the formation of this report, the Committee on Auxiliary Medical Services has felt that it should in large measure be guided by the principles laid down by the House of Delegates of the American Medical Association during the 1937 Convention at Atlantic City.

"The resolution adopted at that time may well be cited here and is appended.

"In the matter of hospital insurance plans it has been alleged that the outstanding obstacle to the formation of a plan satisfactory to the medical profession as well as to the patient and the hospital, is the salaried specialist. In other words, it has been stated that, as long as the hospitals, through the employment of clinical pathologists, roentgenologists, anesthetists, and physical therapeutists as whole or part-time specialists working solely or in part on a salary basis, are thus enabled to furnish patients with such services, it is difficult to object to the furnishing of these same services as a part of a hospital insurance plan.

"Your Committee as a whole is prepared to recognize that there is both some justice and some validity to this contention.

"It is more prepared to do so because it desires to emphasize first, that such financial arrangements are not satisfactory from the standpoints of the specialists concerned; and second, that the existence of this custom is a heritage from the past.

"It seems essential, for the purposes of this discussion, to point out that the specialized departments in question, constitute not only valuable but essential departments of the hospital. Not only are they essential and a vital concomitant of the modern practice of medicine, but they play an important and equally essential part in its continued development.

"It is also essential to recognize that the men engaged in these specialties are, and must be, first of all physicians, and secondly, physicians whose energies and training have been directed toward the attainment of specialized skill in specialties of medical practice as specific and distinct as surgery, obstetrics, or any other specialized entity.

"It is important that this be emphasized, for there has been some tendency in the past, which may even yet still exist in varying degrees, to the effect that the pathologist was merely an individual who made 'tests,' the roentgenologist one who took 'pictures,' the anesthetist one who merely administered a drug, and so on. The corollary to this being that, thus regarded as supernumerary adjuncts, they could, to a greater or lesser degree, be more or less efficiently replaced by technical assistants of greater or lesser training in various technical procedures and manipulations.

"Lest it be thought that this is an extreme or exaggerated viewpoint, it can be maintained with small fear of contradiction

that some such idea, or variation of it, is not infrequent in the minds of some hospital administrators and paradoxical as it may seem—may even be encountered among physicians.

"While it should be unnecessary, it seems nevertheless advisable to recall with some emphasis that the function of the pathologist or the reontgenologist is not, for the one to make 'tests,' or the other 'pictures.' Both are primarily, not only liaison officers between the laboratory and bedside and the patient and the physician, but they may properly be regarded as consultants.

"The real value of the roentgenologist depends, not upon his ability to produce a set of x-ray films, but upon his ability—which, in turn, is dependent upon his ability as a physician—to know *what* examination should be made and how, and most particularly upon his ability to interpret its significance which often involves no mean degree of clinical acumen.

"The real value of the pathologist depends, not upon his facility in technical manipulations nor to supervise their performance by others, but upon his ability to determine, not only which procedure may be most profitably utilized but, especially, upon his ability to interpret its clinical significance and evaluation, which, as before, may demand no small degree of clinical ability.

"The real value of an anesthetist depends, not upon his ability to pour ether or chloroform into an inhaler, to operate a machine for the purpose, or to administer a drug intravenously or by lumbar puncture, but upon his ability to select the method suitable to the particular circumstances and to recognize its dangers, fallacies and limitations; and here, again, without clinical acumen and training the anesthetist is lost—and the patient may well be."

The same principles apply to all similar specialties.

All this being true, as cannot successfully be denied, a salary basis for such specialties is seldom, if ever, satisfactory. First, because the salary is seldom, if ever, commensurate with the importance of the specialty, and, second, because in striking contradistinction to other branches of medicine, no matter how their specialists may increase in skill or reputation, thus becoming a greater and more valuable asset to the institution, the salary has a definitely static tendency and undergoes but infrequent and reluctant changes.

For these reasons, as well as others which obviously develop from the premises laid down above, the Committee strongly deprecates the hamstringing of these specialties of medical practice by the custom more or less generally adhered to, and, by the same token, deprecates with equal emphasis the effect of this situation upon the development of satisfactory plans for hospital insurance.

The Committee desires, therefore, to record its entire accord with the principle *that the services of physicians should not be a part of any plan for hospital insurance*, and to record also its specific and vigorous objection to the inclusion in such plans of the services of pathologists, roentgenologists, anesthetists and physical therapists.

The specific problem before the Committee, however, is not merely to express disapproval of such plans but to propose a working outline that will eliminate medical services from Hospital Insurance Contracts.

It is apparent, of course, that the solution of this problem is neither easy, obvious nor to be rapidly evolved.

From what has been said, it is apparent that these suggestions must embody, first of all, some method whereby the salaried specialists, as such, may be eliminated from the hospital economy. As these various departments differ in their nature and method of functioning, it is necessary that they be separately considered.

*The Department of Radiology*. The practice of radiology in hospitals is essentially

the same as the private practice of this specialty. The radiologist practices his specialty in the same manner as other specialists in the hospital, with the exception that his apparatus is of such a nature that it cannot be moved about readily.

In many instances, the early practice of radiology in hospitals was accomplished by the installation of roentgen equipment by the radiologist, who bore the entire financial burden and received the entire income. The use of hospital space was compensated for by free services to ward patients.

Many changes have occurred since the original plan, and for various reasons either a salary or a commission basis of financial return has been quite generally adopted. In spite of the disadvantages that may have existed under the salary or commission arrangement, affecting either the hospital or the radiologist, an attitude of consideration has been maintained, and on the whole, cordial relationships have been the rule rather than the exception.

However, with the advent of hospital insurance plans, which include radiological services, there has crystallized a definite sense of resistance on the part of radiologists who rightfully feel that their specialty is undergoing exploitation by a third party. Injection of this third party has not only disrupted existing relationships, but has emphasized the necessity for the hospitals to agree to practice hospitalization and to permit the practice of medicine to remain in the hands of those licensed by law to practice medicine.

A solution of the problem that will prevent a third party from injecting itself into medical practice, and at the same time protect the status of radiology in hospital practice, is the one that, in our opinion, is entitled to the support of the Medical Society of New Jersey.

Such a solution is practical under the lease-rental agreement between the hospital and the radiologist. This, in its essentials, is exemplified in the Washington Plan and consists of an arrangement whereby

(1) The radiologist rents space from the hospital, as in an office building, and supplies the equipment and personnel to operate the department

*Or*

(2) The radiologist rents space and leases the equipment by arranging a per examination monthly rebate to the hospital to cover depreciation, obsolescence and overhead.

(3) The radiologist bills the patient direct, on his own billhead, and assumes full responsibility for his financial return, exactly as in private practice.

(4) Should the hospital be obligated to perform free work, the services of the radiologist are contributed free, and the hospital compensates him for the expendable material expense as in examinations of "free patients" and as in the routine examination of internes, pupil nurses and hospital employees.

The lease-rental arrangement for radiological services in hospitals is a workable plan and is in practice in the following hospitals in the United States:

Garfield Hospital, Washington, D. C.

Good Samaritan Hospital, Los Angeles, Calif.

Temple University Hospital, Philadelphia, Pa.

Cottage Hospital, Santa Barbara, Calif.

Queen of Angels Hospital, Los Angeles, Calif.

University of Pennsylvania Hospital, Philadelphia, Pa.

To quote from the report of the Executive Committee of the Pacific Roentgen Club, the advantages of this plan to the hospital and to the radiologist are as follows:

*To the Hospital*

"(a) It puts the relation of the hospital and of certain members of its medical staff on an ethical and equita-

ble basis, encouraging the selection of the radiologist solely on the basis of competence (unbiased by the percentage or salary to which he might agree).

"(b) It removes the question of division of fees, practice of medicine by a corporation, and so forth.

"(c) It insures a more competent type of radiological service without additional cost to the hospital. The radiological department becomes increasingly a 'feeder' to the hospital because of the fact that a good radiologist builds up a clientele of his own and attracts not only good men in the profession to use the hospital, but also hospitalizes many treatment cases of his own.

"(e) It removes from the hospital any question of suit for liability in connection with medical x-ray service and care.

"(f) It provides what is said by one of the most eminent physicians in country, to be the only permanent and satisfactory solution to the problem of hospital radiological work."

*To the Radiologist*

"(a) It places the appointment of the physician-radiologist on the same ethical and legal professional basis as other individual doctors on the staff.

"(b) It removes the question of division of fees.

"(c) It stimulates the hospital radiologist to build up his practice on the proper basis, namely, that of personal skill and ability.

"(d) It places the responsibility for the operation of an efficient radiological practice where it should be placed, namely, with the physician.

"(e) It tends to place the economic status of the radiologist on a level comparable with that of his fellow practitioners and consultants and thereby encourages better men to enter the field."

In consideration of the foregoing, your Committee desires to record the following specific recommendations for the practice of radiology in hospitals in the State of New Jersey.

I. Every hospital radiological department should be under the direction of a competent radiologist, preferably a Diplomate of the American Board of Radiology or one who is working toward that objective.

II. The radiologist should be a member of the senior attending staff.

III. The services of the radiologist should be available, without specific charge to those hospital patients classed as "free patients."

IV. The plan suggested by this Committee eliminates salary or percentage basis arrangements for radiologists in hospitals, and recommends a lease-rental arrangement for space or equipment, or both.

V. In accordance with Resolutions adopted by the American Medical Association, the principles of which are binding upon the component organizations of this Association, radiology should be treated the same as other specialties (surgery, urology, orthopedics, etc.) in any insurance plan.

*Summary*. In recapitulation the consensus of this Committee may thus be summarized:

1. It is in entire accord with the principles laid down by the House of Delegates of the American Medical Association.

2. It is opposed to the inclusion in hospital insurance plans of the services of physicians engaged in specialized phases of the practice of medicine, specifically, clinical pathology, roentgenology, anesthesia and physical therapy.

3. It appreciates the undesirable features of the practice of these specialties on a salary basis.

4. It therefore presents as suggestions for adoption or discussion, various methods whereby this undesirable feature may be eliminated, such methods necessarily varying in connection with the particular specialty involved and being subject to such modifications as may be determined upon between the particular physician and the particular institution involved—always, however, with the provision that such specialties shall not be practiced on a salary basis.

5. It emphasizes the essential necessity, in the event of further consideration of this subject, of including among those to whom this problem may be hereafter presented, representatives of the specialties in question.

MAC F. CAHAL
*Executive Secretary*

Vol. 41, No. 1

# DEPARTMENT OF TECHNIQUE

*Department Editor:* Robert B. Taft, M.D., B.S., M.A., 105 Rutledge Ave., Charleston, S. C.

## AN ADAPTABLE HEADREST FOR SINUS, MASTOID, AND SKULL ROENTGENOGRAPHY

*By* JAMES W. FERGUSON, M.D.
PITTSBURGH, PENNSYLVANIA

HEREWITH is described a device that is quickly and conveniently adaptable for use in sinus, mastoid, and skull roentgenography.

Due to the asymmetrical shape of the head and the irregular location of the parts that frequently require roentgen examinations, numerous different positions in which the head may be placed are necessary in order to depict the various structures in the best possible manner. Each position needs a different-shaped block headrest, or device on which to place the head. The degree angle of the block or headrest differs for the various nasal sinuses and the same device does not work well for roentgenography of the mastoids and other regions about the base of the skull.

To have angle boards or headrests for the many positions required for successful roentgenography of the different regions of the head, in addition to devices for stereoscopic roentgenograms would necessitate the employment of numerous devices which would cost a considerable sum of money, cause more or less inconvenience, and require a greater length of time to obtain just the necessary position and angle for projection of the rays.

In addition, some operators have trouble with the markers. The question as to whether or not the correct marker has been used frequently arises, or the marker is placed on the wrong side of the patient; often it is not registered at all on the film. With the ordinary angle-shaped blocks there are difficulty and inconvenience in centering, positioning, and stabilizing the head.

Frequently the standard or routine examination does not give all the information that is desired in order to make a complete roentgen diagnosis. Sometimes just a little different angle in the projection of the rays through the head is necessary to depict a certain part satisfactorily. At other times duplicates are required for comparative purposes. In some cases, stereoscopic roentgenograms are desired.[1]

The conventional apparatuses are more or less limited as to portability and angle adjustments as well as in centering, positioning, and stabilizing the head and doing stereoscopic work.

With these facts and requirements in mind and with a desire to provide a device permitting easier and more convenient roentgenography of these parts, I developed a headrest which can be adjusted to meet the various positions desired; at the same time, I provided a means for making stereoscopic roentgenograms,[1] together with other convenient features.

This headrest allows the right and left mastoids to be stereoroentgenographed on the same set of films so that both will appear within the stereoscope side by side for comparative study. It contains supports for stabilizing the head. Adjustments are made by sliding them along the slides provided for the purpose. By reversing either support one becomes a localizer and a guide for either the posteroanterior or anteroposterior view of the mastoid, while the other acts as a stabilizer for the head.

Figure 1 is a detail picture which contains a movable grid. The window is sized

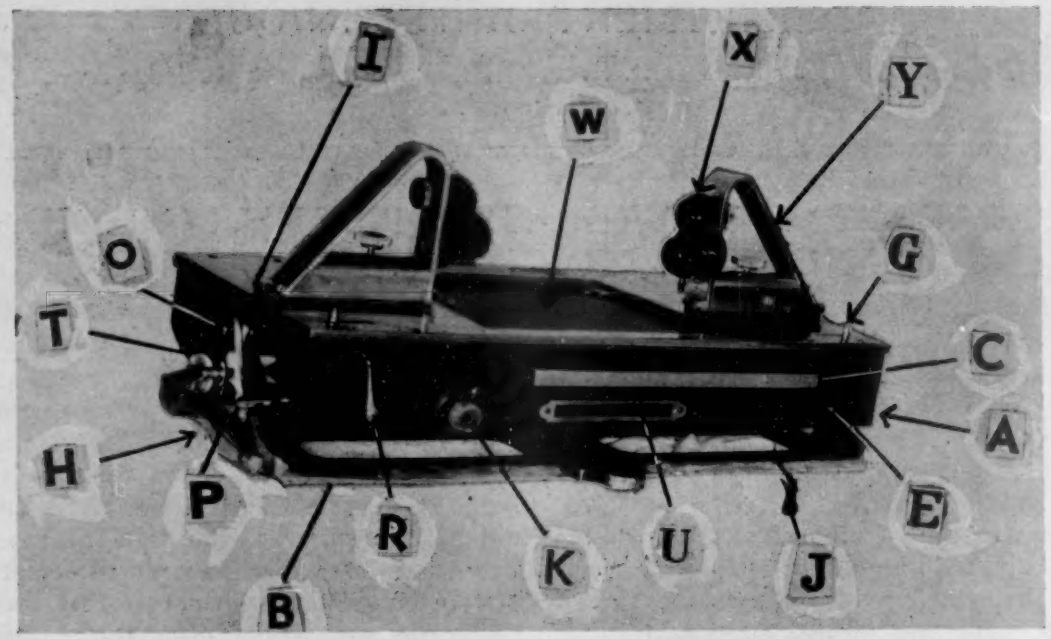


Fig. 1. Headrest with a movable grid. The "reducing mat" is removed.

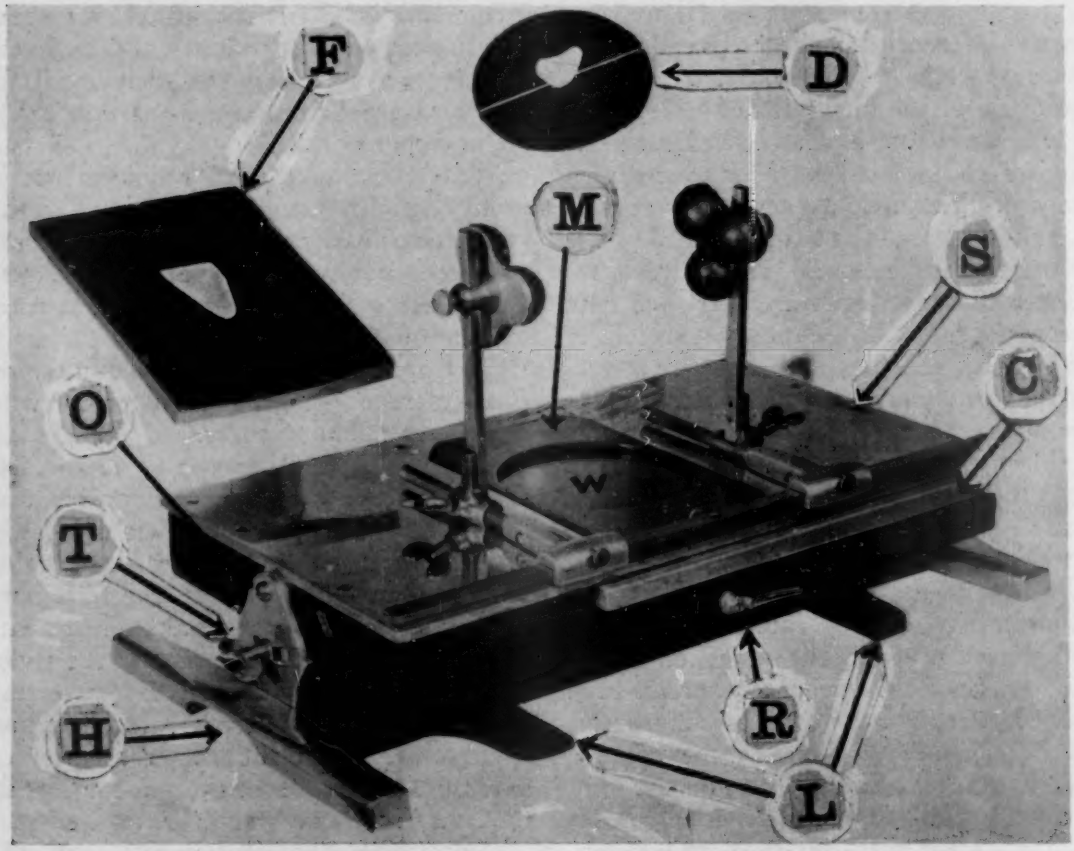


Fig. 2. Headrest without a movable grid.

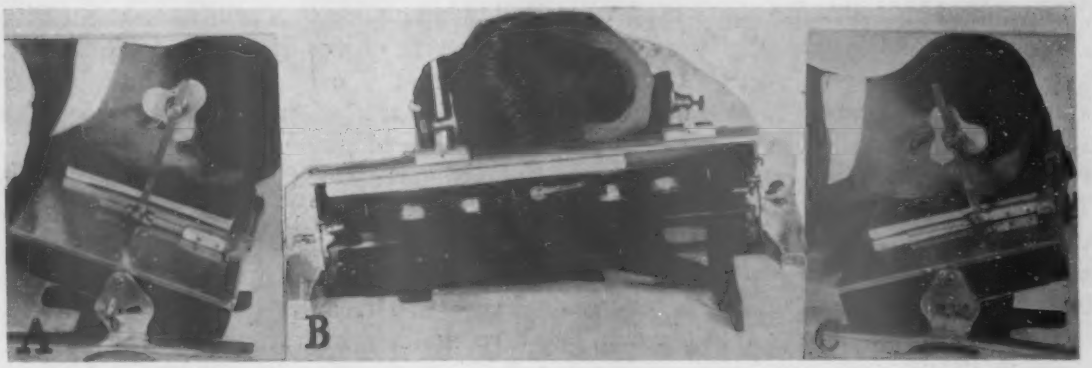


Fig. 3

for an 8 by 10 in. film. A reducing mat similar to *M* (Fig. 2) fits over the window; it reduces the opening to 5 by 7 in. This allows two small views to be made on the same film. It is useful for stereoscopic views of the mastoid, orbit, and sella turcica. Figure 2 shows a similar device without a movable grid. Each comprises a tunnel or box for the casette and film, *C*, mounted above a base which contains folding legs, *L*. The legs may be extended to put the casette tunnel in a sloping position in order to position the head. On the ends of the base are handles, *H*, for portable convenience. The casette tunnel is mounted on the base by a movable joint at a point, *O*, which is on the same level as the film, when enclosed in the casette, ready for the roentgenogram to be made. The method of mounting the casette tunnel above the base permits the casette and its film to be moved on either side of the horizontal plane, which allows for different positions. It is to be noted that many positions can be obtained with but one centering of the central rays. The uprights between the base and the casette tunnel contain thumb locks, *T*, for securely fastening the tunnel in the desired position. The top of the tunnel is made from roentgen opaque material, in the center of which is a window, *W*, covered with a thin fiber material through which the roentgen rays pass to the film. A small mat, *M*, with a circular cut-out, may be placed within the window to aid in centering the object. This mat also permits the edges of the film which surround the image to be darkened by a short exposure to the rays after the insertion of the lead disc, *D*, within its cut-out. The top is made to accommodate a face-rest, *F*, for making roentgenograms in the Granger positions. Notice that stereoscopic roentgenograms in the Granger positions can be conveniently made. This was explained in another article.[2]

The tunnel is provided with a casette lift, *R*, which furnishes a means for lifting the casette and holding it securely against the undersurface of the top of the casette tunnel, thereby reducing to a minimum the object-film distance, and minimizing distortion. The lift also prevents the casette from moving during an exposure or when the tunnel is being adjusted.

A casette tunnel has been provided for taking stereoscopic roentgenograms. A pair of stereograms can be made on one film. By placing the casette at either end of the tunnel, one-half of the film will be exposed under the window. After the first exposure (which is the first eye roentgenogram), the casette is moved to the other end of the tunnel. This procedure places the remaining half of the film under the window for the second exposure (the other eye roentgenogram). It is now obvious that, by using two casettes, both mastoids may be roentgenographed in such a manner that both the right and left mastoids may be viewed within the stereoscope, side by side, for comparative purposes.

The markers shown herein, which were described in another article,[2] are so arranged that in all posteroanterior projections through the face and orbital regions, including the antrums, frontal sinuses, and ethmoid and sphenoid sinuses, the "R" or "L" always appears within the field of exposure but far enough out of the diagnostic field so that it does not interfere with the study of the image. Regardless of whether the "R" or the "L" is placed in the field of exposure the marker letter is always correctly depicted and should remove all doubt, when this system is used, as to whether or not the roentgenograms were correctly marked. The marker letters are placed in reverse so that when roentgenographed they appear in reverse on the film. When the viewer looks upon them in a readable position, this causes him to see them similar to the way in which he would see a patient facing him. When either letter appears in a readable position when viewing the roentgenogram the "R" or "L" will always indicate the correct side of the patient. This system also makes it convenient for placing the films in the stereoscope.[2]

The grid operates on a different principle than does the conventional type, thus allowing a very thin grid to be used, which lessens the object-film distance and permits the grid to be operated in any position. The thickness allows the lead strips to be placed far enough apart to permit tilting of the device for roentgenograms of the mastoid. Quick-acting legs are provided for the purpose. Figure 3*B* shows one leg extended so that the headrest can be tilted. The lead strips are placed parallel to the direction in which the tunnel moves above the base, which allows angling of the headrest 25° on either side of the horizontal plane, permitting sufficient latitude for sinus and mastoid work (Fig. 3*A*, *B*, and *C*).

I do not wish to assume credit for any head position mentioned in this article but merely to introduce a device which is of value in sinus, mastoid, and skull roentgenography.*

REFERENCES

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* Research with these headrests and a new type stereoscopic headtable is in progress at the Falk Clinic of the University of Pittsburgh Medical School. A report will be published in the near future.

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# ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

## ROENTGEN DIAGNOSIS

### NECK AND CHEST

MORELLI, E. Applications de la physiopathologie du poumon à la collapsothérapie. (Application of pulmonary physiopathology to collapse therapy.) *Presse méd.*, Feb. 2, 1938, *46*, 171–173.

Respiratory trauma is the principal cause of the appearance and progression of the phthisiogenic process. The best way to abolish it is by elimination or reduction of the trauma produced by dilatation of the thorax; the same effect may be achieved by any means that restores permeability to the respiratory tract by eliminating stenosis. The latter is at the basis of many general treatments and certain medications. Mountain cures, rest and medications effect their result by slow and quiet respiration, reducing mucus and reducing relative bronchial stenosis. Morelli believes this mechanical effect to be of prime importance.

Complete pneumothorax is the ideal way of eliminating respiratory damage. All other methods of treatment, e.g., operative procedures on the thoracic wall, phrenicectomy, diminution of pathologic and relative stenoses of the respiratory tract tend toward the same result.

Elective pneumothorax, the Jacobeus operation, pneumothoracentesis and alcoholization of intercostal nerves are also discussed from this point of view.—*M. L. Sussman.*

### ABDOMEN

STEUER, KURT. Ueber die Aussenkontour des Magens. (The external contour of the stomach.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, May, 1938, *57*, 467–479.

While modern roentgen methods yield sound information regarding the configuration of the space within the stomach and the details of the inner surface, little attention has been given to the wall itself and particularly to the external outline of the stomach. The outer contour may become particularly evident when the density and thickness of the wall have been increased by carcinomatous infiltration. By using a lower voltage (60 kv.), and a longer exposure time, and a fine focus rotating anode tube, the wall of the stomach can be demonstrated with greater frequency. In the contracted state the stomach wall measures normally 4–5 mm. at the greater curvature and diminishes to 2–3 mm. by moderate filling. Visibility is better when the stomach occupies a transverse position, and in moderately fat individuals because of the contrast offered by peritoneal fat. Ordinarily only the wall of the fornix and greater curvature are demonstrable. An increased width of the gastric wall occurs in severe gastritis. However, the greatest importance of the study of the gastric wall comes in gastric carcinoma when additional information can be gained as to the extent of the lesion and its operability. A number of cases are reported where the usual barium studies were inconclusive and where attention to the outer wall gave evidence of carcinoma at the fundus or fornix.—*W. A. Evans, Jr.*

GOLDEN, ROSS. Antral gastritis and spasm. *J. Am. M. Ass.*, 1937, *109*, 1497–1500.

Because it is the daily task of the roentgenologist to search for causes of digestive disturbance, it seems desirable to examine the roentgen evidence concerning gastritis and to correlate the pathologic changes with those demonstrable by roentgen methods. Gastritis is an inflammation of the gastric wall of as yet unknown etiology which begins in and may be limited to the mucosa but which frequently extends to the deeper layers, even to the serosa. The disease may be generalized but is often limited to or has its maximum effect in the antrum. Gastritis may produce any or all of the symptoms of peptic ulcer, including hemorrhage; pain, vomiting and loss of weight may suggest malignant disease. The diagnosis of gastritis depends mainly on the gastroscopic and the roentgen examination. In many instances the disease can be detected only by gastroscopy. However, in many cases gastritis produces changes in gastric form and function which are demonstrable by the barium sulphate meal.

The normal mucous membrane of the stomach is freely movable over the muscle. In some cases the mucosal folds in the antrum run ir-

regularly transverse to the long axis of the stomach, and when the antral systole takes place they appear to change direction and run parallel with the long axis. For this change to occur, a movement of the mucous membrane in a cephalad direction must take place, thereby stretching it tightly beneath the muscular contractions. In cases of well marked gastritis there are three major disturbances in motility: (1) Peristalsis may be very irregular in depth and in timing or may be absent for long periods. (2) Prepyloric narrowing may be present, sometimes so marked that the antrum appears as a narrow channel, similar to the findings in annular infiltrating carcinoma. (3) Pylorospasm may be present. As a result of these disturbances the emptying of the stomach may be greatly delayed. It seems logical to assume that antral spasm is the result of inflammation of the gastric wall, which is present in prepyloric narrowing either with or without ulcer or mucosal erosion. At the present time the evidence strongly favors the opinion that gastritis is an important factor in the cause of hypertrophy of the pyloric muscle. The most important roentgen sign of hypertrophy of the pyloric muscle is elongation of the pyloric channel with preservation of the mucosal folds. When prepyloric spasm is also present, the proximal limits of the channel may not be identified, and the diagnosis may only be suspected.

Much difficulty is encountered by both roentgenologists and surgeons in differentiating antral gastritis and its complications from carcinoma. The difficulty is enhanced for the roentgenologist by the fact that infiltrating carcinoma does not necessarily obliterate completely contractions of the muscle. The most important differential point is the demonstration by pressure methods or otherwise of mucosal folds in the narrowed area which should be obliterated by infiltrating carcinoma. If atrophic gastritis has caused a thinning of the mucous membrane and an absence of folds, the diagnosis becomes very difficult. A definite palpable mass corresponding under the roentgenoscope to the antrum should be considered as evidence in favor of malignant disease. The author has never been much impressed with the effect of atropine in differential diagnosis, but he has found that repetition of the examination after several days of gastric lavage, particularly if definite stasis is present, has been helpful.

In summarizing, the author states that antral gastritis is associated with Kaufmann's "prepyloric syndrome," and that this syndrome consists of (1) prepyloric narrowing due to spasm; (2) abnormal, stiff, irregular peristalsis; (3) sometimes exaggeration and sometimes diminution or absence of mucosal folds; (4) hypertrophy of the pyloric muscle; (5) shallow mucosal erosions, or penetrating ulcer of the lesser curvature; (6) delay in emptying, sometimes resulting in a twenty-four hour gastric residue.—*S. G. Henderson.*

Pape, R. Zur Differentialdiagnose blutender Magentumoren. (The differential diagnosis of bleeding gastric tumors.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, March, 1938, *57*, 286–295.

The problems of diagnosis in 7 unusual cases are presented. The first was a woman, aged sixty-eight, who showed clinically anacidity and occult bleeding, and the roentgen appearance indicated a small polyp. Pathologically the lesion was simply a benign hypertrophy of the mucous membrane. The second case also showed clinical evidence of a malignant tumor and the roentgen study indicated a small irregular defect which at operation proved to be adenocarcinoma. In the third case there was an incidental roentgen finding of a large tumor at the cardia. No operation was performed, but the appearance was unchanged after one year and was assumed to be due to a submucous fibroma. The fourth case exhibited clinically hematemesis, pallor, and weight loss. Roentgen study showed two polypoid gastric tumors, one being the size of an apple with an irregular border. Histologically the lesion was an adenocarcinoma. Case v showed clinically occult bleeding and anacidity, and roentgenologically a large irregular polypoid mass with superficial ulceration on the greater curvature, the malignant nature of which was confirmed by the palpation of liver metastasis. Case vi was a woman aged seventy, who for many years had noticed a large smooth mobile mass in the mid abdomen and for a short time had complained of anorexia, inanition, and pallor. The roentgen examination showed a large mass in the antrum with a sharply localized defect, the interpretation being a benign tumor with a peptic ulceration. Under treatment the ulceration disappeared and over a period of four years no change occurred in the appearance of the large mass. The seventh case was a man with a rapidly growing tumor in the left hypochondrium. Roentgen study showed a large tumor at the cardia on the

greater curvature in which there was a fistulous tract. Autopsy revealed a myosarcoma with central degeneration. Thus, bleeding in gastric tumors may be (1) the result of mechanical irritation of small epithelial defects; (2) superficial erosions which are usually cancerous, but may occur in tuberculosis, leukemia, or lymphogranuloma; (3) deep erosions with dish-shaped craters which form the most common type of ulceration in tumors; (4) peptic ulceration at the crest of benign tumors; (5) fistulous ulcerations, as in Case VII and, (6) bleeding from varices which produce a tumor-like mass in the fornix of the stomach. While the roentgenologist can give reliable information concerning the morphology of a process, he cannot give the histological character. Therefore, every apparently benign tumor which bleeds must be kept under careful observation.—*W. A. Evans, Jr.*

GYNECOLOGY AND OBSTETRICS

HAMBLEN, E. C., BAKER, R. D., and DERIEUX, G. D. Roentgenographic diagnosis and anatomic studies of a quintuple pregnancy. *J. Am. M. Ass.*, July 3, 1937, *109*, 10–12.

Quintuple pregnancy is expected about once in forty million births, according to calculation by the Hellin ratio. The case described by the authors makes the total of reported cases thirty-five. This is apparently the first instance in which a diagnosis has been made prior to delivery.

A white woman, aged twenty, was hospitalized because of hydramnios and irregular bleeding complicating a pregnancy of approximately five months' duration. A roentgenogram of the abdomen in the lateral position showed the presence of four fetal heads and five bodies. Labor was induced because of continued uterine bleeding and elevation of the maternal pulse rate to 120 per minute. Heart action in two fetuses continued for thirty minutes after birth. One of the five was an anencephalic monster. The placenta was oval. Inspection showed no evidence of subdivision. There was apparently a separate amnion for each fetus. The four well-formed fetuses had similar genitalia of female type, while the external genitalia of the monster were like those of the other fetuses but more rudimentary.

The chief interest in the reported case lies in the fact that the diagnosis was made from the roentgenogram and that the circumstances allowed a complete anatomic study of the fetuses, placenta and membranes. The chief discussion provoked by the anatomic studies is in regard to whether this pregnancy was uniovular or multiovular. When a single placenta occurs in a multiple pregnancy, several criteria have been laid down to determine whether the pregnancy is derived from a single ovum or not. Among the more important of these are the presence of a single chorion, the anastomosis of blood vessels among the various cord attachments, and the similarities of fetuses with regard to sex and peculiarities of structure. The authors feel that this pregnancy may well have been derived from a single ovum, but definite proof is lacking.—*S. G. Henderson.*

GENITOURINARY SYSTEM

RITVO, MAX, and STEARNS, DAVID B. Roentgen diagnosis of contusions of the kidney. *J. Am. M. Ass.*, Oct. 2, 1937, *109*, 1101–1105.

Mild injuries to the kidney are important to the practitioner in view of their frequency, because they may lead to the invalidism of chronic or recurrent infection and in some instances to subsequent formation of stone. The diagnosis in severe cases is not difficult, the syndrome of pain, hematuria and prostration after a blow to the loin giving a characteristic clinical picture. Diagnosis of injury to the kidney in cases of mild trauma has heretofore been much more difficult. This type of trauma, with only moderate injury to the kidney, doubtless accounts for pain and lameness of the back which incapacitate the patient for an inordinate length of time. Heretofore it has been generally recognized that the clinical manifestations of mild renal trauma are meager, variable and not definitely diagnostic. Roentgenologically, also, renal trauma has not been satisfactorily demonstrable unless ruptures or tears of considerable degree existed. The present communication is concerned with a roentgenographic method of diagnosis in cases of mild or moderate injuries to the kidney and is applicable particularly to contusions of the kidney without severe tears or ruptures of the renal tissues.

Injuries to the kidney may result from direct or indirect trauma. These injuries vary from slight traumas to very severe rupturing or tearing wounds. Owing to the edema and the accumulation of oozing blood, the calyces and renal pelvis are compressed and the upper portion of the ureter is displaced mediad and sometimes upward. Roentgen examination should

be carried out in all cases unless contraindicated by the severity of the injury. The flat roentgenogram may give helpful information occasionally. One may see haziness, or apparent enlargement of the renal shadow; absence or blurring of the outlines of the psoas muscle; fixation or limitation of mobility of the kidney; fracture of the lower ribs or transverse processes of the lumbar vertebrae; and scoliosis. In pyelographic studies, the retrograde method is usually the more satisfactory. Extensive ruptures which communicate with the pelvis and calyces are shown by extravasation of the opaque medium into the kidney parenchyma or subcapsular tissues. The authors have observed definite roentgen appearances after mild or moderate injuries on the basis of which a diagnosis may be made. Characteristic changes in the renal pelvis, calyces and ureter are demonstrable on the pyelogram. The ureter in cases of contusion of the kidney is pushed toward the vertebral column, forming an arc. The normal narrowings, dilatations and curves of the upper part of the ureter are obliterated. The ureteropelvic junction may be displaced upward. The kidney pelvis is narrowed and flattened along its inferior border. The calyces and infundibula become depressed and distorted. The demonstration of these changes in the renal pelvis, calyces and ureter in conjunction with a history of trauma is positive evidence of contusion of the kidney, but the absence of these signs does not exclude renal injury. In the differential diagnosis one must consider renal neoplasm, tuberculosis of the kidney, infections of the kidney and ureter and perinephric abscess.—*S. G. Henderson.*

Kretschmer, Herman L. and Kanter, Aaron E. Effect of certain gynecologic lesions on the upper urinary tract; a pyelographic study. *J. Am. M. Ass.*, Oct. 2, 1937, *109*, 1097–1101.

In several previous communications it was demonstrated that, during pregnancy and the puerperium, dilatation of the ureters and kidney pelves occurred in 100 per cent of cases, that there was a return to normal in 59.3 per cent after two weeks and in 34.3 per cent after six weeks, and that the remaining 6.2 per cent were normal after twelve weeks. The striking fact about the dilatation of the ureter during pregnancy is that, with rare exceptions, it is above the brim of the pelvis. It was also found that lateral displacement of the ureters, when found early in pregnancy, tends to increase as the pregnancy advances.

In the selection of cases for the present study, the authors used patients who had no urinary symptoms and who were normal on urinary examination so that they might demonstrate how frequently changes are found in this so-called silent or asymptomatic group. Cases presenting carcinoma were not included. As a routine, intravenous pyelography was carried out, diodrast being the agent selected. This was supplemented by retrograde pyelograms in a few instances.

There were 24 cases of fibroids above the brim of the pelvis. Seventeen of these demonstrated a pathologic condition in the upper urinary tract, whereas 7 were completely normal. There were 11 cases of fibroids below the brim of the pelvis. Six of these presented pathologic changes in the pyelogram and 5 were normal. There were 11 cases of ovarian cyst. Nine showed changes in the upper urinary tract and only 2 appeared normal. Of the 4 cases of prolapse, 3 appeared normal and only 1 showed bilateral dilatation. The pyelograms were negative in the 1 case of tubo-ovarian abscess studied. The changes in the pelves varied in degree from unilateral dilatation of the pelvis alone or dilatation of the pelvis and calyces to very extensive dilatation and clubbing of the calyces. The changes in the ureters consisted of unilateral or bilateral dilatation and unilateral or bilateral displacement of the ureters, or a combination of the two. Irrespective of the type of gynecologic lesion present, the dilatation, when found, was above the brim of the pelvis, with the exception of one case in which the pelvic ureter was dilated down to the vesical end. In this case a diagnosis of true stricture of the ureter at the vesical end was made, thus taking it out of this category of cases.

In view of the fact that 9 of the 11 cases of ovarian cyst showed changes in the pyelogram, it is reasonable to assume that the consistency of the tumor and its ability to mold or compress has something to do with the high incidence of these changes. In the large fibroids above the brim of the pelvis, 70.9 per cent showed changes in the ureteropyelograms. In the cases in which there was dilatation, it was found at operation that the fibroid so molded the pelvis that it probably compressed the ureter with resulting dilatation. In fibroids below the brim of the pelvis, changes in the upper urinary tract were produced in 6 out of 11 cases.

Following appropriate surgical procedure, a return to normal took place in 72.5 per cent of these cases. In the small group of patients who still showed changes at the time of discharge from the hospital, subsequent check-up pyelograms showed a return to normal. Failure to appreciate the frequency with which these lesions occur is due to the fact that there has been no routine preoperative study in the group of cases that do not present urinary symptoms and urinary signs.—*S. G. Henderson.*

LAMARQUE, P., GUIBAL, A., and BETOULIERES, P. Accidents d'iodisme aigu au cours d'une pyélographie intraveineuse. (Acute iodism during intravenous pyelography.) *Bull. et mém. Soc. d'électro-radiol. méd. de France*, Jan., 1938, *26*, 78–80.

Reactions have occurred in two classes of patients: (1) those with severe organic disease, cardiac, hepatic or renal; (2) immediate reactions in individuals with apparently normal urinary tracts. Shock phenomena sometimes occur which are peculiar and are occasionally suggestive of iodism.

Von Jaschke reported a case of severe glottic edema; Tepson reported a case of tetanic crisis; Truchot, a case of laryngeal crisis with tetanic spasm and exitus by axphyxia in a few minutes.

The present case is that of a boy, aged nine, about one year after a complete rupture of a kidney which was successfully repaired. The blood urea was 0.30 gm. per liter. There was no sugar nor albumin in the urine. There were rare red blood cells, no white cells and no casts.

Ten cubic centimeters of 35 per cent per abrodil (about one-half the average adult dose) was injected in three minutes. Two to three minutes after injection the boy reddened; there were conjunctival congestion, sneezing, coughing and dyspnea. Urticaria appeared rapidly, vomiting of mucus and passage of normal stool. The pulse was rapid and at times imperceptible. Heart sounds were difficult to hear; cyanosis followed. These symptoms lasted fifteen minutes, then slowly disappeared leaving weakness. Satisfactory roentgenograms of the pelvis and calyces were obtained at the twenty-five-minute period. The shock symptoms could be due to the effect of the hypertonic solution injection. The urticaria and mucous membrane congestion suggested iodism.—*M. L. Sussman.*

### NERVOUS SYSTEM

SCHMID, BERNHARD. Sur Frage der röntgenologisch fassbaren Veränderungen an der Wirbelsäule bei Rückenmarkstumoren. (Changes in the spine detectable roentgenologically in spinal cord tumors.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, March, 1938, *57*, 299–305.

The author uses the method of Elsberg and Dyke in studying the interpeduncular spaces in 19 expanding lesions involving the spinal cord. Definite aid in localization was obtained in 63.7 per cent of the cases. Measurements also give an indication of the extent of the lesion which may not be obtained by myelography. Malignant extradural tumors may reveal their nature by the character of the localized destruction of the pedicle. Extradural tumors are accompanied by a lower incidence of interpeduncular space changes than the juxtamedullary tumors.—*W. A. Evans, Jr.*

### SKELETAL SYSTEM

THOMSON, JOHN. A case of the Klippel-Feil syndrome. *Arch. Dis. Childhood*, April, 1937, *12*, 127–131.

Thomson reports a case of the Klippel-Feil syndrome occurring in a girl, aged four. This condition, as originally described by Klippel and Feil, consists of (1) a numerical variation of the vertebrae; (2) more or less fusion between the bony elements of the cervical vertebrae; (3) accompanied sometimes by spina bifida or other congenital abnormalities. The cause of the condition has not yet been defined. All that can be said is that it is essentially an intra-uterine condition. It does not appear to be hereditary.

The most prominent symptom is the short neck. As a result a low hair line is seen at the back of the neck and there is a distinct depression at the nape of the neck. The shortness of the neck is exaggerated by a kyphosis which is present in the dorsal region. The scapulae tend to be higher than usual and the head is usually thrown forward as though the bony skeleton were not able to support it. In extreme cases the chin may actually rest on the thorax. The head movements are limited and there is some muscle spasm of the cervical muscles. Disturbance of breathing may be present in the form of obstruction such as is seen in cases of hypertrophied adenoids. There may also be difficulty in swallowing. Torticollis may also occur.

The condition must be differentiated from Sprengel's deformity, ordinary wryneck and tuberculosis of the vertebrae.

The roentgenogram of Thomson's case showed the tip of the spine of the seventh cervical vertebra fused with those of the first and second thoracic vertebrae; the sixth cervical was flattened from above downward and its body was fused to the fifth cervical above it; the bony elements comprising the fifth, fourth, third and second cervical vertebrae were displaced forward for a distance of one-quarter of an inch and their common fused spine was in contact with the base of the skull; the odontoid process of the second cervical vertebra was fused with the posterior aspect of the anterior transverse arch of the first cervical vertebra.—*R. S. Bromer.*

Logròscino, D. Dyschondroplasie (Dyschondroplasia.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Feb., 1938, *57*, 131–142.

The concept of dyschondroplasia can be used to cover a wide variety of roentgenographic and clinical states and has been enlarged by some to include epiphysitis, the fluted form of osteopoikilosis, osteogenic exostoses, and multiple enchondroma. While differentiation of the former two is easy, more difficulty arises with the others. The similarity of dyschondroplasia, osteogenic exostoses, and multiple enchondroma has been recently emphasized by numerous authors and the whole group has been called chondrodystrophy. Differences in the three forms are shown in the hereditary tendency (greater in osteogenic exostoses), prevalence of changes in the growing metaphysis, occurrence in adults (most common in multiple enchondroma), and shortening of the extremities (most marked in dyschondroplasia). According to Ollier, dyschondroplasia is always unilateral, affecting the epiphyses and metaphyses of the growing long bones. The author and many others do not subscribe to this.

Dyschondroplastic tissue is shown histologically to be formed by hyalin cartilage which is proliferative in the periphery and degenerative centrally. The ossifying cortical portions show signs of resorption while more new bone is forming. When this destruction and formation of bone are not coordinated, the cartilage proliferates and breaks out and is then not covered by ossifying cortex.

The patient usually comes to the physician because of mild pain, deformity or shortening of an extremity, or because of knobby thickening of some part of the skeleton. The roentgen examination alone can determine the type and distribution of the disease and should always include the entire skeleton. With numerous illustrations the author describes a variety of conditions showing the similarities and interrelations. The changes are, of course, most marked during the period of active growth and the involution phase sets in with the end of skeletal growth.

The etiology and pathogenesis are still obscure and little can be added to the writings of Ollier (1899). The process is one of abnormal proliferation of cartilage derived from the growth cartilage and has nothing in common with neoplastic tissue. The disease ends with the full growth of the skeleton. Dyschondroplasia is not hereditary, and familial or past diseases are not important. Bentzon held the view that there is a primary vasomotor disturbance of vegetative nervous system origin, but was unable to obtain satisfactory experimental evidence. Also, there is no clinical evidence of abnormality of the vegetative nervous system as might be expected in the hemiplegic cases. Others have sought to incriminate the pyramidal tracks or the endrocrine glands without much success. More likely the disease is of congenital origin due to an unknown cause which operates in the embryonal development.—*W. A. Evans, Jr.*

Feistmann-Lutterbeck, E. Die Röntgendiagnostik des Kretinenbeckens und der Osteoarthrosis cretinosa. (The roentgen diagnosis of the cretin pelvis and of osteoarthrosis cretinosa.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, May, 1938, *57*, 506–514.

Looser first described the condition of cretin hip, but no carefully correlated roentgen and clinical studies have been carried out on a large group. Normal hips are rarely seen in cretins. Three grades of changes are described in adults. In Grade I there is slight flattening and broadening of the femoral heads with corresponding changes in the acetabulum and a shortening of the femoral necks with a high position of the trochanters which have a knobby, plump appearance. There may also be unossified apophyses at the iliac crests or ischial tuberosities and developmental disturbance at the synostosis of the pubic and ischial bones. In Grade II advanced changes of the same sort are seen and in addition alteration of the shape of the pelvis resulting from the fact that during development there has been disturbance primarily in the enchondral ossification. In Grade III

changes in the bone structure become apparent as irregular areas of rarefaction and sclerosis in the femoral head. In late stages secondary deforming arthritic changes occur at the hip joints. This osteoarthrosis cretinosa was found in 62 per cent of the cases of dwarf cretins with atrophic thyroid glands and in 22 per cent of those with goiter. These changes are to be differentiated from those seen in Perthes' disease, arthritis deformans, and osteochondritis dissecans.

The predominant change in children is a delay in the osseous development which may reach extreme degrees. The case of a twelve-year-old cretin is illustrated, who showed an osseous development of one year. Not only is there delay but the ossification occurs irregularly, beginning in different centers, and at the femoral epiphysis the appearance may resemble Perthes' disease. The coxa vara deformity results from the predominance of periosteal bone growth. Developmental disturbance is demonstrable in about 70 per cent of cretins without goiters and in 30 per cent of those with goiters. —*W. A. Evans, Jr.*

ROBERTS, FFRANGCON. Secondary carcinoma of bone. *Lancet*, June 18, 1938, *1*, 1378–1382.

The author emphasizes our lack of knowledge as to the intermediate stages of carcinomatous dissemination. We are inclined to view the presence of metastasis as a terminal event. Yet evidence of metastasis may not be found until years after radical removal of the primary lesion. What has been the activity of the residual neoplasm during such an interim? Moreover, the response by many of these lesions to roentgen therapy should dispel undue pessimism as to their presence.

Even in the case of carcinoma, metastatic dissemination, distant to the primary lesion, in most instances would appear to take place by way of the blood stream. The commonest carcinomas to form distant metastases in the skeleton include breast, kidney, prostate and thyroid. The fact that such spread from primary lesions in the uterus, ovary, rectum and pharynx is less commonly seen might not always be attributable to any inherent differences in the capacity of such tissues to metastasize but instead to the fact that those primary growths, because of their locations, may kill before metastasis has taken place. Metastases are more likely to be found in bone, liver, and brain; they are rarely found in the spleen. Skeletal muscle, tendon, and cartilage appear to be immune. Breast neoplasms show a particular affinity to bone; lung shows an unusually high proportion of secondaries in the brain and spinal cord. Within the skeleton there appear to be certain favorable sites for metastasis. For instance, the thyroid shows a tendency to select the skull. Post-mortem studies would indicate that otherwise the commonest sites include: the spine (especially lumbar), upper end of the femur, pelvis, skull and ribs. The author believes that in the case of breast metastasis, at least, the main incidence is "in those parts of the skeleton through which the weight of the body is transmitted and which first show senile changes." The interval between the discovery of a primary and evidence of secondary metastases may vary considerably; it may be as long as fourteen years. Particularly in the case of the kidney and the prostate, secondary lesions may be found before there is any realization of the primary.

Pain is always prominent. It may vary in type, perhaps suggesting a "lumbago" or a "sciatica." In most cases the diagnosis is established roentgenographically, though symptoms may develop a short while before roentgen criteria become evident.

Considered pathologically, osteoclastic metastasis has been found to fill the haversian canals and surround the bony trabeculae. Bone is eroded and its space is occupied by tumor cells and reaction fibrosis. The actual osteoclasis appears to take place at some distance from the neoplastic cells; it appears to be due to the reaction process—a fibrosis. There is considerable death of neoplastic cells due to obliteration of the vessels by them. In the case of osteoblastic metastases, osseous tissue appears to be stimulated to proliferation. It would seem that the essential difference between these two types "is solely one of reaction." Considerable reasoning is presented to emphasize the belief that dissemination of these metastases is more likely by way of the vascular system, rather than by way of the lymphatics. The authors believe that most of the scattered cells are either attenuated or overcome by normal cells, especially in the capillaries of the lungs. He does not believe many cases of dissemination should be blamed upon surgical manipulations; instead he thinks that presurgical manipulations, even by the patient, are more likely responsible. He strongly recommends roentgen therapy, citing the relief of pain and restoration of working

capacity—for months and even years. He employs 200 kv., filtered through 1 mm. Cu plus 1 mm. Al; the dosage varies but, for the lumbar region, he would use portals of about 10×15 cm., distance 40 cm. and cross-firing from obliquities, would administer 1,000 to 1,200 r through each, over a period of ten days (thereby giving 500 to 800 r to the bone itself). If symptoms are not relieved by this dosage, more is given through anterior oblique portals, but in all the total dosage is less than would be given a primary lesion—for "metastases are usually more radiosensitive than the primary tumors from which they arise." Several case examples are cited.—*A. A. de Lorimier.*

Allott, E. N., and Jemson, J. Generalised osteitis fibrosa due to a retro-oesophageal parathyroid tumour. *Lancet*, March 12, 1938, *1*, 609–611.

A case of parathyroid deossification is presented to emphasize the dire state which might be reached without recognition of the entity and to insist that with substantial clinical and roentgenological evidence, careful surgical exploration should be made until the tumor is located. The patient was a girl, aged nineteen, who had first noted some aching of her right arm and a prominence of the clavicle. She had been operated upon at another institution with "reconstruction of the sterno-clavicular joint." Later, she developed pains in both arms and both legs, and muscular weakness developed to such an extent that she was unable to stand alone. When examined, she could barely lift her legs off of the bed and she could not lift against resistance. There was slight tenderness to pressure over the bones. Roentgenography revealed widespread deossification, with conspicuous rarefaction of the ribs and clavicles; a mottled decalcification of the skull; cyst-like areas in the ilia; partial fracture of the right pubis and irregular and delayed union of the epiphyseal junctions of both ascending rami; general mottled decalcification of both humeri; cyst-like rarefactions in the 4th and 5th metacarpals, on both sides, etc. The serum calcium was 15.5 mg. per 100 cc.; later it reached to 17.3 mg. An exploratory operation of the neck was performed. For some time no tumor could be found; the inferior parathyroids were located and they appeared normal but finally with digital examination in the wound a tumor was felt behind the esophagus at the level of the 7th cervical and 1st thoracic vertebrae. This was removed and identified as an adenomatous hyperplasia of a parathyroid. The day after the operation the patient complained of stiffness of the face and tingling in the limbs. Positive Chvostek and Trousseau signs continued for ten days. Muscular power was restored so that after twenty-five days she was able to walk alone. The day after the operation, the blood calcium fell to 11.3 mg. per 100 cc.; the next day, to 9.5 mg. The plasma phosphatase had been 1.1 units per cc. (normal 0.1 to 0.2) and continued above normal even nine months after the operation.)—*A. A. de Lorimier.*

Coryn, G. Les affections endocriniennes du squelette. (Endocrinological affections of the skeleton.) *Presse méd.*, 1938, *46*, 228.

The thyroid influences all phases of enchondral ossification. Hypothryoidism in infancy is accompanied by a delay in growth proportional to the thyroid deficiency. The adult individual is a dwarf who is disproportionate, dysharmonic and sometimes asymmetrical. The dwarfism is moderate (90–140 cm.), the limbs being shorter than the trunk. Dysharmony is due to excessive head volume, saddle nose, and the shoulders being carried back. The joints are large for the length of the diaphyses. Asymmetry occurs when the deformity of the joints is more marked on one side than on the other.

Roentgenography is a precise method of investigation. The age of the skeleton is retarded as compared with the age of the subject. The difference may reach five to six years. At about the age of twenty-two, retardation in union is less marked and at twenty-four to twenty-six disappears. Now a new growth impulse occurs.

Hyperthyroidism is much more rare in infancy. The affected individuals grow rapidly but growth is arrested precociously by premature union. The adult is of smaller build than normal.

Each time that thyroid function becomes excessive, a diffuse generalized osteoporosis takes place. Blood calcium and phosphorus are normal, phosphatase is moderately increased. Urinary calcium is increased. A study of the calcium balance gives contradictory information. The daily loss of calcium seems to be slightly elevated (0.100 gr.). The determination of calcium balance cannot pretend to great accuracy. The duration of the sickness appears more important than its gravity. Osteoporosis can be seen roentgenographically only when the skeleton has lost 10/100 of its calcium, but de-

calcification is found in all cases of hyperthyroidism of some duration.

In hypothyroidism of infancy there are articular lesions, particularly of the hips, knees and shoulders. Roentgen examination shows a flattened articular head. Deformed and irregular cartilage is abundant. The head of the bone shows a series of clear spaces throughout irregularly dense epiphyses. These are cartilaginous islands. If the thyroid assumes a normal function at puberty as sometimes happens, the joint deformities may be the only residue. Hyperthyroidism has been thought responsible for certain cases of deforming and ankylosing arthritis in old women as shown by narrowing of the interspace, disappearance of cartilage, irregularities of the surfaces and adjacent osteoporosis. The hyperthyroid origin is logically possible but proof is difficult.

Cartilaginous changes in hypothyroid conditions are due to deficiency of cellular proliferation which explains the retarded ossification. In hyperthyroidism the process is accelerated. Lacunar resorption is marked and osteoclasis exaggerated. In hypothyroidism the bone is firm to cut, the cortex is thick, the medulla is crossed by heavy bone outlined by osteoblasts and osteoclasts are rare. In the zone of provisional calcification the calcified cartilage is thin but denser than normal. There is a fibrous and myxomatous degeneration of the hyaline casts. The disturbance in ossification tends to remain.

We have no knowledge of the changes in hyperthyroidism. Thyroidectomy leads to change of hypothyroidism in the skeleton. Small doses of thyroid leads to acceleration of growth; larger doses to diminution.

The results of hyperthyroidism are discussed. —*M. L. Sussman.*

Buttinger, Therese. Ueber multiple zystoide Knochentuberkulose. (Multiple cyst-like osseous tuberculosis.) *Fortschr. a. d. Geb. d. Röntgenstrahlen*, Feb., 1938, *57*, 176–183.

The clinical picture described by Kienböck is characterized by a predominance in children, and by the multiple cyst-like character of the lesions occurring chiefly in the cortex and epiphyseal portions of the skeleton. The course is benign, periostitis is rare and bone atrophy slight. Jüngling's "Ostitis tuberculosa multiplex cystoides" is also a sharply delimited clinical picture, including all types of multiple cyst-like osseous tuberculosis. This latter type occurs chiefly in the phalanges, metatarsals and metacarpal bones. The author reports the case of a boy, aged eight and a half, with forty separate foci of tuberculosis in the skeletal system. The lesions appeared all about the same time, that is three-quarters of a year after a primary pulmonary parenchymal lesion which later subsided. The lesions tended to be symmetrical and with secondary involvement of neighboring joints. The spine and hip joints were not affected. The tubercle bacilli were isolated by animal inoculation, thus establishing the diagnosis, and were shown to be a human type of normal virulence. Some of the lesions were cyst-like in character and involved the phalanges, long bones (particularly about the elbow joint when there was marked periosteal reaction) and the middle ribs, but also such rare sites as the mandible, scapula, and patella. Considered in the differential diagnosis were osteopathia fibrosa cystica and neoplastic metastases. The author does not feel that his case fits either the description of Jüngling's ostitis or of Kienböck's disease.—*W. A. Evans, Jr.*